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=> s (insulin()like()growth()factor()binding()protein()5) or
(IGF()binding()protein()5) or IGFBP5 or (IGFBP()5) or IBP5 or (ibp()5)

5 FILES SEARCHED...

L1 2494 (INSULIN(W) LIKE(W) GROWTH(W) FACTOR(W) BINDING(W) PROTEIN(W)
5) OR (IGF(W) BINDING(W) PROTEIN(W) 5) OR IGFBP5 OR (IGFBP(W)
5) OR IBP5 OR (IBP(W) 5)

=> s l1 and (antisens? or ribozym? or triplex)

L2 84 L1 AND (ANTISENS? OR RIBOZYM? OR TRIPLEX)

=> dup rem l2

PROCESSING COMPLETED FOR L2

L3 42 DUP REM L2 42 DUPLICATES REMOVED)

=> d l3 ikib aks tot

13 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1001:314936 CAPLUS

DOCUMENT NUMBER: 136:321257

TITLE: Use of pregnancy-associated plasma protein A2
(PAPP-A2), a novel **insulin-like**

growth factor-binding

protein-5 proteinase, for diagnosis
and treatment of fetal abnormalities

INVENTOR(S):

PATENT ASSIGNEE(S):

SOURCE:

Oxvig, Claus; Ivergaard, Michael Toft
Comp Biotech Aps, Den.
PCT Int. Appl., 113 pp.
1001:314936

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032953	A2	20020425	WO 2001-DK695	20011019

W: AB, AC, AD, AE, AF, AG, AH, AI, AJ, AK, AL, AM, AN, AO, AP, AQ, AR, AS, AT, AU, AV, AW, AX, AY, AZ, BA, BB, BC, BD, BE, BF, BG, BH, BI, BJ, BK, BL, BM, BN, BO, BP, BQ, BR, BS, BT, BU, BV, BW, BX, BY, BZ, CA, CB, CC, CD, CE, CF, CG, CH, CI, CJ, CK, CL, CM, CN, CO, CP, CQ, CR, CS, CT, CU, CV, CW, CX, CY, CZ, DA, DB, DC, DD, DE, DF, DG, DH, DI, DJ, DK, DL, DM, DN, DO, DP, DQ, DR, DS, DT, DU, DV, DW, DX, DY, DZ, EA, EB, EC, ED, EE, EF, EG, EH, EI, EJ, EK, EL, EM, EN, EO, EP, EQ, ER, ES, ET, EU, EV, EW, EX, EY, EZ, FA, FB, FC, FD, FE, FF, FG, FH, FI, FJ, FK, FL, FM, FN, FO, FP, FQ, FR, FS, FT, FU, FV, FW, FX, FY, FZ, GA, GB, GC, GD, GE, GF, GG, GH, GI, GJ, GK, GL, GM, GN, GO, GP, GQ, GR, GS, GT, GU, GV, GW, GX, GY, GZ, HA, HB, HC, HD, HE, HF, HG, HH, HI, HJ, HK, HL, HM, HN, HO, HP, HQ, HR, HS, HT, HU, HV, HW, HX, HY, HZ, IA, IB, IC, ID, IE, IF, IG, IH, II, IJ, IK, IL, IM, IN, IO, IP, IQ, IR, IS, IT, IU, IV, IW, IX, IY, IZ, JA, JB, JC, JD, JE, JF, JG, JH, JI, JJ, JK, JL, JM, JN, JO, JP, JQ, JR, JS, JT, JU, JV, JW, JX, JY, JZ, KA, KB, KC, KD, KE, KF, KG, KH, KI, KJ, KK, KL, KM, KN, KO, KP, KQ, KR, KS, KT, KU, KV, KW, KX, KY, KZ, LA, LB, LC, LD, LE, LF, LG, LH, LI, LJ, LK, LL, LM, LN, LO, LP, LQ, LR, LS, LT, LU, LV, LW, LX, LY, LZ, MA, MB, MC, MD, ME, MF, MG, MH, MI, MJ, MK, ML, MN, MO, MP, MQ, MR, MS, MT, MU, MV, MW, MX, MY, MZ, NA, NB, NC, ND, NE, NF, NG, NH, NI, NJ, NK, NL, NM, NO, NP, NQ, NR, NS, NT, NU, NV, NW, NX, NY, NZ, OA, OB, OC, OD, OE, OF, OG, OH, OI, OJ, OK, OL, OM, ON, OO, OP, OQ, OR, OS, OT, OU, OV, OW, OX, OY, OZ, PA, PB, PC, PD, PE, PF, PG, PH, PI, PJ, PK, PL, PM, PN, PO, PP, PQ, PR, PS, PT, PU, PV, PW, PX, PY, PZ, QA, QB, QC, QD, QE, QF, QG, QH, QI, QJ, QK, QL, QM, QN, QO, QP, QQ, QR, QS, QT, QU, QV, QW, QX, QY, QZ, RA, RB, RC, RD, RE, RF, RG, RH, RI, RJ, RK, RL, RM, RN, RO, RP, RQ, RR, RS, RT, RU, RV, RW, RX, RY, RZ, SA, SB, SC, SD, SE, SF, SG, SH, SI, SJ, SK, SL, SM, SN, SO, SP, SQ, SR, SS, ST, SU, SV, SW, SX, SY, SZ, TA, TB, TC, TD, TE, TF, TG, TH, TI, TJ, TK, TL, TM, TN, TO, TP, TQ, TR, TS, TU, TV, TW, TX, TY, TZ, UA, UB, UC, UD, UE, UF, UG, UH, UI, UJ, UK, UL, UM, UN, UO, UP, UQ, UR, US, UT, UV, UW, UX, UY, UZ, VA, VB, VC, VD, VE, VF, VG, VH, VI, VJ, VK, VL, VM, VN, VO, VP, VQ, VR, VS, VT, VU, VV, VW, VX, VY, VZ, WA, WB, WC, WD, WE, WF, WG, WH, WI, WJ, WK, WL, WM, WN, WO, WP, WQ, WR, WS, WT, WU, WV, WW, WX, WY, WZ, XA, XB, XC, XD, XE, XF, XG, XH, XI, XJ, XK, XL, XM, XN, XO, XP, XQ, XR, XS, XT, XU, XV, XW, XX, XY, XZ, YA, YB, YC, YD, YE, YF, YG, YH, YI, YJ, YK, YL, YM, YN, YO, YP, YQ, YR, YS, YT, YU, YV, YW, YX, YY, YZ, ZA, ZB, ZC, ZD, ZE, ZF, ZG, ZH, ZI, ZJ, ZK, ZL, ZM, ZN, ZO, ZP, ZQ, ZR, ZS, ZT, ZU, ZV, ZW, ZX, ZY, ZZ.

PRIORITY APPLN. INFO.:

DK 2000-1571 A 20001030
US 2000-241840P P 20001020

AB The present invention provides nucleotide and amino acid sequences that identify and encode a new protein with homol. to pregnancy-associated plasma protein-A (PAPP-A). We denote this protein PAPP-A2. The cDNA encoding PAPP-A2 was derived from human placenta. The present invention also provides for **antisense** mols. to the nucleotide sequences which encode PAPP-A2 and expression vectors for the prodn. of purified PAPP-A2. Antibodies, capable of binding specifically to PAPP-A2, and hybridization probes or oligonucleotides for the detection of PAPP-A2-encoding nucleotide sequences are also provided. Genetically engineered host cells

for the expression of PAPP-A2 and use of the protein to produce antibodies

capable of binding specifically to the protein are another embodiment of the present invention. Methods of screening for pathologies in pregnant and non-pregnant patients that are based on detection of PAPP-A2 antigen in human body fluids or PAPP-A2-encoding nucleic acid mols are provided. Use of the protein to screen for agents that alter the protease activity of PAPP-A2, use of the protein as a therapeutic target for such agents, and use of the protein as a therapeutic agent in relevant pathol. states are other objects of the invention. Methods for screening for altered focal proliferation states in pregnant and/or non-pregnant patients,

which

include detecting levels of PAPP-A2, are also described. The present invention also provides the identification of a natural substrate of PAPP-A2, insulin-like growth factor binding protein (IGFBP)-

5.

L3 ANSWER 2 OF 42 USPTFULL

ACCESSION NUMBER: 2002:98890 USPTFULL

TITLE: HER -2/neu overexpression abrogates growth inhibitory pathways

INVENTOR(S): Slamon, Dennis J., Woodland Hills, CA, UNITED STATES
Wilson, Cindy A., Los Angeles, CA, UNITED STATES
Galsbol, Frank J., Westlake Village, CA, UNITED STATES
PATENT ASSIGNEE: The Regents of the University of California and Amgen Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002051735	A1	20020502
APPLICATION INFO.:	US 2001-813517	A1	20010320 (3)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-190598P	20000320 (10)

NUMBER OF CLAIMS: 24
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 10 Drawing Pages
 LINE COUNT: 2765

AB The present invention provides methods for obtaining genetic profiles of

cancer cells in order to assess the status of a cancer in an individual.

In addition, the present invention provides methods for inhibiting the growth of cancer cells that exhibit certain genetic profiles. These methods identify an important link between HER-2/neu overexpression and loss of growth inhibition by the TGF-beta signaling pathway in cancer cells. Compositions as well as therapeutic and diagnostic methodologies based on this disclosure are provided.

L3 ANSWER 3 OF 41 USPATEFULL

ACCESSION NUMBER: 2002:16859 USPATEFULL
 TITLE: Metastatic breast and colon cancer regulated genes
 INVENTOR(S): Grese, Klaus, Berlin, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002009789	A1	20020124
APPLICATION INFO.:	US 2001-827669	A1	20010406 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-417615, filed on 18 Oct 1999, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-104351P	19991015 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Chiron Corporation, Intellectual Property R338, P.O. Box 8097, Emeryville, CA, 94662-8097	
NUMBER OF CLAIMS:	20	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3011	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Gene sequences as shown in SEQ ID NOS: 1-85 have been found to be significantly associated with metastatic potential of cancer cells, especially breast and colon cancer cells. Methods are provided for determining the risk of metastasis of a tumor, which involve determining whether a tissue sample from a tumor expresses a polypeptide encoded by a gene as shown in SEQ ID NOS: 1-85, or a substantial portion thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 42 USPATEFULL

ACCESSION NUMBER: 2002:85934 USPATEFULL
 TITLE: Polynucleotides, polypeptides expressed by the polynucleotides and methods for their use
 INVENTOR(S): Watson, James L., Auckland, NEW ZEALAND
 Murison, James G., Auckland, NEW ZEALAND
 PATENT ASSIGNER(S): Genesis Research & Development Corporation Ltd., NEW ZEALAND (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6390360	B1	20020430
APPLICATION INFO.:	US 2000-724804		20001128 (9)

PRIORITY INFORMATION: US 1999-171678P 19991222 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: GRAFEE
PRIMARY EXAMINER: Carlson, Karen Cochrane
ASSISTANT EXAMINER: Mitra, Rita
LEGAL REPRESENTATIVE: Speckman, Ann W., Sleath, Janet
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 2
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 3737

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel polynucleotides including partial and extended sequences, and open reading frames, are provided, together with probes and primers, DNA constructs comprising the polynucleotides, biological materials and organisms incorporating the polynucleotides, polypeptides expressed by the polynucleotides, and methods for using the polynucleotides and polypeptides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

LE ANSWER 5 OF 42 USPATEFULL

ACCESSION NUMBER: 2002:75188 USPATEFULL
TITLE: Methods and compositions for identifying morphogenic protein analogs using morphogenic protein responsive inhibitory elements
INVENTOR(S): Yeh, Lee-Chuan C., San Antonio, TX, United States
Lee, John C., San Antonio, TX, United States
PATENT ASSIGNEE(S): Syntex Corporation, Kalamazoo, MI, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6368737	B1	20020409
APPLICATION INFO.:	US 1999-465353		19991216 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Riley, Mezia		
LEGAL REPRESENTATIVE:	Fish & Neave, Haley, Jr., James F., Mangasarian, Karen		
NUMBER OF CLAIMS:	14		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	12 Drawing Figure(s); 13 Drawing Page(s)		
LINE COUNT:	1687		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates generally to methods and compositions for identifying morphogenic protein analogs. In one embodiment, this invention relates to an osteogenic protein responsive transcription inhibitory element. This invention also relates to the identified morphogenic protein analogs which can mimic the biological effects of morphogenic proteins, particularly those relating to the BMP family such as osteogenic proteins (OP-1), on the regulation of gene expression and tissue inductive capabilities.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

LE ANSWER 6 OF 42 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:63856 CAPLUS
DOCUMENT NUMBER: 134:125934
TITLE: **IGFBP-5 antisense**
oligonucleosynucleotide therapy for hormone-regulated tumors

SOURCE: PCT Int. Appl., 45 pp.
CONTIN: PIXXD2
DOCUMENT TYPE: P
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005435	A2	20010125	WO 2000-CA353	20000719
WO 2001005435	A3	20010322		

W: AE, AG, AL, AM, AP, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CY, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MN, MW, MX, MY, MZ, ND, NE, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, EG, KE, MD, RU, TJ, TM

EW: BR, BM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SH, TD, TG

EP 1200573	A2	20020112	EP 2000-947725	20000719
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: US 1998-144495P P 19990719
WO 2000-CA353 W 20000719

AB A method is provided for treating hormone-regulated tumors (e.g. breast and prostatic tumors) in mammals, including humans, by administration of an **antisense** oligodeoxynucleotide (ODN) which is complementary to a portion of the gene encoding **IGFBP-5**. Using the Shionogi tumor model in vitro and in vivo, the administration of such an ODN was shown to reduce proliferation of tumor cells, and also to delay the progression to androgen independence. Thus, treatment of prostate cancer in mammals, including humans, and delay of the progression of prostate tumors to androgen independence is accomplished by administering to the mammal a therapeutically effective amt. of an **antisense** oligodeoxynucleotide which is complementary to a portion of the nucleic acid sequence encoding **IGFBP-5** and which hybridizes with such a sequence to inhibit expression of **IGFBP-5**. Specific **antisense** ODNs which are suitable for use in the method are GACCACGCTGATCACCAT, which is derived from the murine gene sequence, and CGCGGTGAGCAACACCAT and AGGTCATGCAGCAGCGGC, which are derived from the human gene sequence.

L3 ANSWER 7 OF 42 USPATFULL

ACCESSION NUMBER: 2001:231143 USPATFULL

TITLE: Arrays for identifying agents which mimic or inhibit the activity of interferons

INVENTOR(S): Silverman, Robert H., Beachwood, OH, United States
Williams, Bryan R. G., Cleveland, OH, United States
Der, Sandy, Cleveland, OH, United States

PATENT ASSIGNEE(S): The Cleveland Clinic Foundation, Cleveland, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6331396	B1	20011218
APPLICATION INFO.:	US 1998-405438		19990323 (P)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-101497P	19980923 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	

NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 963
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and model systems for identifying and characterizing new therapeutic agents, particularly proteins, which mimic or inhibit the activity of all interferons, Type I interferons, IFN-.alpha., IFN-.beta., or IFN-.gamma.. The method comprises administering an interferon selected from the group consisting of IFN-.alpha., IFN-.beta., IFN-.tau., IFN-.omega., IFN-.gamma., and combinations thereof to cultured cells, administering the candidate agent to a duplicate culture of cells; and measuring the effect of the candidate agent and the interferon on the transcription or translation of one or, preferably, a plurality of the interferon stimulated genes or the interferon repressed genes (hereinafter referred to as "ISG's" and "IPGs", respectively). The model system is an array with gene probes that hybridize with from about 100 to about 5000 ISG and IRG transcripts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

LS ANSWER 8 OF 42 USPATFULL
ACCESSION NUMBER: 2001:214830 USPATFULL
TITLE: TNF receptor death domain ligand proteins and inhibitors of ligand binding
INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schievella, Andrea R., Winchester, MA, United States
Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6322972	B1	20011127
APPLICATION INFO.:	US 1998-185258		19981102 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-839032, filed on 23 Apr 1997, now patented, Pat. No. US 5891675 Division of Ser. No. US 1996-698551, filed on 15 Aug 1996, now patented, Pat. No. US 5712381, issued on 27 Jan 1998 Continuation-in-part of Ser. No. US 1996-602223, filed on 15 Feb 1996, now patented, Pat. No. US 5843675 Continuation-in-part of Ser. No. US 1995-533901, filed on 26 Sep 1995, now patented, Pat. No. US 5852173 Continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995, now patented, Pat. No. US 5849501 Continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	ELT, John		
LEGAL REPRESENTATIVE:	Lahive & Cockfield, LLP, Mandragouras, Esq., Amy E.		
NUMBER OF CLAIMS:	21		
EXEMPLARY CLAIM:	-		
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)		
LINE COUNT:	1637		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are disclosed. Methods of making and using the ligand proteins and methods of making

TNF-RI-III ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 9 OF 42 USPATFULL

ACCESSION NUMBER: 2001:71356 USPATFULL

TITLE: Methods for the production of biologically active agents contained in an extracellular matrix

INVENTOR(S): Keeping, Hugh S., 10 King Philip Ave., Bristol, RI, United States 02809

	NUMBER	FIND	DATE
PATENT INFORMATION:	US 6232121	B1	20010515
APPLICATION INFO.:	US 2000-580109		20000530 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-137368P	19990603 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Ketter, James	
LEGAL REPRESENTATIVE:	Hifer, Mark A. Brown, Rudnick Freed & Gesmer	
NUMBER OF CLAIMS:	25	
EXEMPLARY CLAIM:	1	
LINE COUNT:	715	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for the production in vitro of cell growth supportive surfaces comprising naturally secreted human extracellular matrix material comprising biologically active agents such

as growth factors ideally produced and elaborated by the extracellular matrix-secreting cells. The present invention provides an efficient method for improving growth factor potency and extending half-life in order to promote cell attachment, growth and/or differentiation. The surfaces of the present invention enable propagation of difficult cells in culture.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 10 OF 42 USPATFULL

ACCESSION NUMBER: 2001:44198 USPATFULL

TITLE: Treatment of partial growth hormone insensitivity syndrome

INVENTOR(S): Attie, Kenneth M., San Francisco, CA, United States
Carlsson, Lena M. S., Gothenburg, Sweden
Gesundheit, Neil, Los Altos, CA, United States

PATENT ASSIGNEE(S): Reddard, Audrey, San Francisco, CA, United States
Genentech, Inc., South San Francisco, CA, United States

U.S. Corporation

	NUMBER	FIND	DATE
PATENT INFORMATION:	US 6207640	B1	20010327
APPLICATION INFO.:	US 1996 648212		19960503 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-410452, filed on 24 Mar 1995, now abandoned Continuation of Ser. No. US 1994-224982, filed on 7 Apr 1994, now patented, Pat. 6,111,111		

PRIMARY EXAMINER: Jones, Dwayne C.
ASSISTANT EXAMINER: Delapoint-Muirneid, C.
LEGAL REPRESENTATIVE: Knoke, Martens, Olson & Bear, LLP
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 44 Drawing Figure(s); 38 Drawing Page(s)
LINE COUNT: 2465

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for increasing the growth rate of a human patient having partial

growth hormone insensitivity syndrome, but not Laron syndrome, are described. One such method comprises administering an effective dose of growth hormone, preferably growth hormone with a native human sequence, with or without an N terminal methionine, to the patient. The patient

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characterized as having a height of less than about -2 standard deviations below normal for age and sex, a serum level of high-affinity growth hormone binding protein that is at least 2 standard deviations below normal levels, a serum level of IGF-I that is below normal mean levels, and a serum level of growth hormone that is at least normal. In another such method, the same patient population is treated with an effective amount of IGF-I, given alone or in combination with an amount of growth hormone that is effective in combination with the IGF-I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 11 OF 42 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001388936 MEDLINE
DOCUMENT NUMBER: 21336417 PubMed ID: 11412654
TITLE: Novel therapeutic strategy for advanced prostate cancer using **antisense** oligodeoxynucleotides targeting anti-apoptotic genes upregulated after androgen withdrawal to delay androgen-independent progression and enhance chemosensitivity.
AUTHOR: Miyake H; Hara I; Kamidono S; Gleave M E
CORPORATE SOURCE: The Prostate Center, Vancouver General Hospital, Vancouver, Canada.. hideakimiyake@hotmail.com
SOURCE: INTERNATIONAL JOURNAL OF UROLOGY, (2001 Jul) 8 (7) 337-49. Ref: 61
Journal code: CE6; 9440137. ISSN: 0919-8172.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
REVIEW LITERATURE.
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 1.0110
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20011008
Entered Medline: 20011004

AB Progression to androgen-independence remains the main obstacle to improving survival for patients with advanced prostate cancer. In this review, findings are summarized that have recently been demonstrated to establish novel therapeutic strategy targeting several genes playing functionally important roles after androgen withdrawal and during androgen independent progression. The authors initially characterized changes in gene expression after androgen withdrawal in the androgen-dependent Shionogi and LNCaP tumor models using cDNA arrays. Based on these results, they focused on genes highly upregulated after androgen ablation (i.e. bcl-2, bcl-xL, TR.FM-2, **IGFBP-5**), which have anti-apoptotic or mitogenic activities, and thereby confer

a

resistance to androgen withdrawal as well as cytotoxic chemotherapy. The

cancer through the inhibition of target gene expression, resulting in a delay in the progression to androgen-independence by enhancing apoptotic cell death induced by androgen ablation and chemotherapy. The authors

also

showed the effectiveness of combined **antisense** CDN therapy and cytotoxic chemotherapy by achieving additive or synergistic effects.

These

findings provide a basic significance for the design of clinical studies using **antisense** CDN either alone or in combination with chemotherapeutic agents in patients with advanced prostate cancer.

L3 ANSWER 12 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:424131 BIOSIS

DOCUMENT NUMBER: PFEV200100424131

TITLE: The IGF/IGFBP system in CNS malignancy.

AUTHOR(S): Zumkeller, W. (1); Westphal, M.

CORPORATE SOURCE: (1) Department of Pediatrics, Martin-Luther-University Halle-Wittenberg, University Hospital, Ernst-Grube-Str.

40,

16097, Halle/Saale: walter.zumkeller@medizin.uni-halle.de Germany

SOURCE: Molecular Pathology, (August, 2001) Vol. 54, No. 4, pp. 227-239. print.
ISSN: 1366-8714.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The insulin-like growth factor (IGF) system includes IGF-I and IGF-II, the

type I and type II IGF receptors, and specific IGF binding proteins (IGFBP-1 to IGFBP-6). These factors regulate both normal and malignant brain growth. Enhanced expression of IGF-I and IGF-II mRNA transcripts

has

been demonstrated in gliomas, meningiomas, and other tumours. Abnormal imprinting of IGF-II occurs in gliomas, medulloblastomas, and

meningiomas.

Both types of IGF receptor are expressed in gliomas and, in particular, the type I IGF receptor appears to be upregulated in malignant brain tissue. **Antisense** IGF-I receptor mRNA induces an antitumour response, resulting in complete brain tumour regression. Clinical trials for the treatment of brain tumours in humans based on a gene transfer protocol using IGF-I receptor **antisense** are under way. All six IGFBPs are expressed to a variable extent in brain tumours. High concentrations of IGFBP-2 are found in cerebrospinal fluid from patients with malignant central nervous system tumours; therefore, IGFBP-2 might

be

a useful marker for these tumours. IGFBP-4 appears to be a negative regulator of tumour proliferation. Both in vitro and in vivo experiments suggest that the IGF system represents an important target for the treatment of malignant central nervous system tumours and the ongoing trials should provide valuable information for future therapeutic approaches.

L3 ANSWER 13 OF 42 USPATFULL

ACCESSION NUMBER: 2001:77189 USPATFULL

TITLE: Mouse arrays and kits comprising the same

INVENTOR(S): Chenchik, Alex, Palo Alto, CA, United States

Lukashev, Matvey, Newton, MA, United States

PATENT ASSIGNEE(S): Clontech Laboratories, Inc., Palo Alto, CA, United States (U.S. corporation)

NUMBER

KIND

DATE

on 31 Mar 1998
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Marschel, Ardin H.
LEGAL REPRESENTATIVE: Field, Bret E. Bozicevic, Field & Francis, LLP
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 1451

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Mouse arrays and methods for their use are provided. The subject arrays include a plurality of polynucleotide spots, each of which is made up of

a polynucleotide probe composition of unique polynucleotides corresponding to a key mouse gene. The subject arrays find use in hybridization assays, particularly in assays for the identification of differential gene expression of key mouse genes of interest.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

LE ANSWER 14 OF 42 USPATEFULL

ACCESSION NUMBER: 2000:13550 USPATEFULL
TITLE: Insulin-like growth factor binding protein (IGFBP-6)
INVENTOR S : Kiefer, Michael C., Clayton, CA, United States
Maslany, Frank R., San Francisco, CA, United States
Zupf, Jurgen Johann Leopold, Zurich, Switzerland
Born, Walter Hans, Zurich, Switzerland
PATENT ASSIGNEE(S): Chiron Corporation, Emeryville, CA, United States
U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6025465		20000215
APPLICATION INFO.:	US 1997-917204		19970825 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1990-576648, filed on 31 Aug 1990, now abandoned which is a division of Ser. No.		

US 1990-574613, filed on 28 Aug 1990, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Carlson, Karen Cochrane
LEGAL REPRESENTATIVE: Perkins & Associates, Guth, Joseph H., Blackburn, Robert

P.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 1789

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A purified binding protein selected from the group consisting of insulin-like growth factor binding protein having an amino acid sequence

which is at least 95% homologous to the amino acid sequence of FIG. 1 and fragments thereof comprising at least 11 consecutive amino acids of the sequence that are capable of binding to an antibody specific for the

protein or to an insulin-like growth factor is described. Recombinant DNA molecules encoding the binding proteins and subsequences thereof are

also described along with recombinant microorganisms and cell lines containing the DNA molecules and methods for preparing the binding proteins by growing the recombinant hosts containing the relevant DNA molecules. Antibodies to the protein, identified as IGFBP-6, which are also described.

13 ANSWER 15 OF 42 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 200030630 MEDLINE
DOCUMENT NUMBER: 20306630 PubMed ID: 11650457
TITLE: Castration-induced up-regulation of **insulin-**

like growth factor
binding protein-5 potentiates
insulin-like growth factor-I activity and accelerates
progression to androgen independence in prostate cancer
models.

AUTHOR: Miyake H; Pollak M; Gleave M E
CORPORATE SOURCE: The Prostate Centre, Vancouver General Hospital, British
Columbia, Canada.
SOURCE: CANCER RESEARCH, 2000 Jun 1; 60 (11): 3053-64.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STM: 20000714
Last Updated on STM: 20000714
Entered Medline: 20000630

AB Although **insulin-like growth factor**
binding protein-5 (IGFBP-5
) has been shown to be implicated in prostate cancer progression, the
functional role of **IGFBP-5** in progression to
androgen-independence remains largely undefined. Here, we demonstrate
substantial up-regulation of **IGFBP-5** during
castration-induced regression and androgen-independent (AI) progression

in
the mouse androgen-dependent (AD) Shionogi tumor model. To analyze the
functional significance of these changes in **IGFBP-5**,
human AD LNCaP prostate cancer cells were stably transfected with
IGFBP-5 gene, and **IGFBP-5**
-overexpressing LNCaP tumors progressed significantly faster to androgen
independence after castration compared with controls. **Antisense**
mouse **IGFBP-5** oligodeoxynucleotides (ODNs) were then
designed that reduced **IGFBP-5** expression in Shionogi
tumor cells in vitro in a dose-dependent and sequence-specific manner.
Growth of Shionogi tumor cells was inhibited by **antisense**
IGFBP-5 ODN treatment in a time- and dose-dependent
manner, which could be reversed by exogenous IGF-I. However,
antisense IGFBP-5 ODN treatment had no
additive inhibitory effect on Shionogi tumor cell growth when IGF-I
activity was neutralized by anti-IGF-I antibody. **Antisense**
IGFBP-5 ODN treatment resulted in decreased
mitogen-activated protein kinase activity and number of cells in the S +
G2-M phases of the cell cycle that directly correlated with reduced
proliferation rate of Shionogi tumor cells. Systemic administration of
antisense IGFBP-5 ODN in mice bearing Shionogi
tumors after castration significantly delayed time to progression to
androgen independence and inhibited growth of AI recurrent tumors. These
findings suggest that up-regulation of **IGFBP-5** after
castration serves to enhance IGF bioactivity and raise the possibility
that the response of prostate cancer to androgen withdrawal can be
enhanced by strategies, such as **antisense IGFBP**
5 ODN therapy, that target IGF signal transduction.

13 ANSWER 16 OF 42 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000458689 MEDLINE
DOCUMENT NUMBER: 20400567 PubMed ID: 10942528
TITLE: Increased expression of IGF-binding protein-5 in Luchenne

AUTHOR: Melone M A; Peluso G; Galderisi U; Petillo D; Cotrufo R
CORPORATE SOURCE: Second Division of Neurology, Second University of Naples,
Anatomy Medicine, Naples, Italy..

marina.melone@unina2.it

SOURCE: JOURNAL OF CELLULAR PHYSIOLOGY, (2000 Oct) 185 (1): 143-53.
Journal code: HNB; 005012... ISSN: 0021-9541.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200008

ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001011
Entered Medline: 20001925

A5 In DMD the progressive loss of muscle ability and concomitant increasing
fibrosis might originate from, besides other causes, the fibroblast
paracrine inhibition of satellite cell "growth." In this study we report
that in myoblast/fibroblast coculture experiments, the presence of DMD
fibroblasts negatively interfered with DMD myoblast growth to an extent
directly proportional to the percentage of DMD fibroblasts present in the
mixed-cell cultures. Moreover, the observation that media conditioned

with

proliferating DMD fibroblasts inhibited the growth of DMD myoblasts more
seriously than did control fibroblast-conditioned media suggested a
paracrine effect by diffusible factors. IGF-binding proteins could act as
such diffusible factors; in fact, **IGFBP-5** transcript
increased threefold in DMD fibroblasts proliferating in DMD muscle
extracts, whereas IGFBP-3 mRNA decreased. In addition, high levels of
IGFBP-5 protein were detected in DMD
fibroblast-conditioned media. In neutralizing **IGFBP-5**
in DMD fibroblast-conditioned media by means of specific antibodies, or
inhibiting **IGFBP-5** gene expression in DMD fibroblasts
by means of oligo **antisense**, the fibroblast-conditioned media
lost inhibitory power over DMD myoblast proliferation.
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LE ANSWER 17 OF 42 MEDLINE DUPLICATE 4

ACCESSION NUMBER: 2000411425 MEDLINE

DOCUMENT NUMBER: 20021327 PubMed ID: 10562152

TITLE: Mesenchymal-epithelial transition in the developing
metanephric kidney: gene expression study by differential
display.

COMMENT: Erratum in: Genesis 2000 Jul;27(3):136

AUTHOR: Plisov S Y; Ivanov S V; Yoshino K; Dove L F; Elisova T M;
Higinbotham K G; Karavanova I; Lerman M; Perantoni A C

CORPORATE SOURCE: Laboratory of Comparative Carcinogenesis, National Cancer
Institute, Frederick, Maryland 21702-1201, USA..
plisov@mail.ncifcrf.gov

CONTRACT NUMBER: N01-CN-56000 (NCI)

SOURCE: GENESIS, (2000 May) 27 (1): 22-21.
Journal code: DK7; 100931242. ISSN: 1526-954X.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENEANK-AW672633; GENEANK-AW672634; GENEANK-AW672635;
GENEANK-AW672636; GENEANK-AW672637; GENEANK-AW672638;
GENEANK-AW672639; GENEANK-AW672640; GENEANK-AW672641;
GENEANK-AW672642; GENEANK-AW672643; GENEANK-AW672644;
GENEANK-AW672645; GENEANK-AW672646; GENEANK-AW672647

AB The developing metanephric kidney is a convenient model to study molecular

events associated with epithelial cell differentiation. To determine the genes involved in the defining event of this process, namely, the conversion of metanephric mesenchyme to the epithelium of the nephron, we applied differential display (DD) techniques. Explants of rat metanephric mesenchymes were induced to condense *ex vivo* with fibroblast growth

factor

2 (FGF2) or to form tubules with FGF2 and conditioned medium (CM) from a cell line (RUB1) of ureteric bud, the renal inductive tissue. Three time points (6, 24, and 72 h) were chosen to track the dynamics of gene expression during morphogenesis. Seventy-two up- or down-regulated mRNAs were identified, including 36 novel sequences and those of cell cycle regulatory proteins (TGF-beta2, Cyclin D1, p57Kip2), transcription

factors

(beta-catenin, Sox11, D91), signaling proteins (SH3-domain binding protein, G-protein-coupled receptor, Ser-Thr protein kinase), cell adhesion molecules (syndecan-4, integrin-beta1), and also gene33, H19, SMO, IGFBP5, MAMA receptor, lectin, keratin, beta-tubulin, calreticulin, GRP78, ERp72, MnSOD, thioredoxin, and others. Some have previously been associated with kidney development and serve as good controls for expected changes, while most have not been linked with

kidney

epithelial cell differentiation. Using thin sections of embryonic kidney and labeled **antisense** PNA probes, we applied RNA hybridization to confirm the results of DD and related the expression of these genes to specific cell lineages of the developing kidney. These results provide a window into the events that mediate this critical differentiation process and suggest that a limited number of interrelated events direct the epithelial conversion of metanephric mesenchyme. *genesis* 27:32-31, 2000. Published 2003 Wiley-Liss, Inc.

L3 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:708627 CAPLUS

DOCUMENT NUMBER: 131:341964

TITLE: Compositions and methods for extending the action of clostridial neurotoxin and modulating neurite outgrowth in damaged neural endplates

INVENTOR(S): Dally, J. Oliver; Acki, Kei Roger; De Paiva, Anton

PATENT ASSIGNEE(S): Allergan Sales, Inc., USA

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9855459	A1	19991104	WC 1999-US8303	19990415
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NC, NL, NO, NZ, PT, PG, RU, SE, SG, SI, SK, SL, TD, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, A2, BY, BG, BR, CH, CL, CU, DE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9837484	A1	19991116	AU 1999-37484	19990415
EP 1073455	A1	20010227	EP 1999-319857	19990415
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, RU, SK, TR, UA, UG, UZ, VN, YU, ZW, AM, A2, BY, BG, BR, CH, CL, CU, DE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

TM

AB Methods and compns. are disclosed for modulating neurite outgrowth in damaged neural endplate. Also disclosed are methods for extending the period during which tissue treated with Clostridial toxin is paralyzed.
 REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L3 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:421772 CAPLUS

DOCUMENT NUMBER: 131:68554

TITLE: Insulin-like growth factor binding protein fragments and their use in diagnosis and therapy

INVENTOR(S): Forssmann, Wolf-Georg; Standker, Ludger; Khendorf, Maik; Kling, Lothar; Spitz, Hans-Georg; Mostafavi, Hossein

PATENT ASSIGNEE(S): Germany

SOURCE: PCT Int. Appl., 02 pp.

CODEN: FIKXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832620	A1	19990701	WO 1998-EP8405	19981222
W: CA, JP, US				
EW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19757250	A1	19990701	DE 1997-19757250	19971222
CA 2315974	AA	19990701	CA 1998-2315974	19981222
EP 1042476	A1	20001011	EP 1998-965865	19981222
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE, IE				
JP 2002508931	T2	20020326	JP 2000-525539	19981222
PRIORITY APPLIN. INFO.:				
			DE 1997-19757250 A	19971222
			WO 1998-EP8405	W 19981222

OTHER SOURCE(S): MARPAT 131:68554

AB The invention relates to peptides which are derived from insulin-like growth factor binding protein (IGFBP). The invention also relates to cyclic, glycosylated, phosphorylated, acetylated, amidated and/or sulfatized derivs. of these peptides. The peptides may be isolated from hemofiltrate or urine. Thus, an IGFBP-2 fragment was isolated from hemofiltrate and this peptide complexed with IGF was shown to have a neuroprotective effect on PC-12 cells. In addn., an IGFBP-4 fragment was found to stimulate proliferation of osteoblasts.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L3 ANSWER 20 OF 42 USPATFULL

ACCESSION NUMBER: 1999:106316 USPATFULL

TITLE: TNF receptor death domain ligand protein.

INVENTOR(S): Lin, Lih-ling, Concord, MA, United States

Chen, Jennifer, Chestnut Hill, MA, United States

Schlevella, Andrea R., Winchester, MA, United States

Branam, James, Somerville, MA, United States

PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5948638		19990907
			19990907 (A)

continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995, now patented, Pat. No. US 5849501

which

is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Peisee, Lila
ASSISTANT EXAMINER: Kaufman, Claire M.
LEGAL REPRESENTATIVE: Sprunger, Suzanne A., Brown, Scott A.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s) ; 8 Drawing Page(s)
LINE COUNT: 2138

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing

the TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

13 ANSWER 11 OF 42 USPATFULL

ACCESSION NUMBER: 1999:43423 USPATFULL
TITLE: TNF receptor death domain ligand proteins
INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schievella, Andrea R., Winchester, MA, United States
Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5891675		19990406
APPLICATION INFO.:	US 1997-839032		19970413 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1996-693551, filed on 15 Aug 1996, now patented, Pat. No. US 5712381, issued on 27 Jan 1998 which is a continuation-in-part of Ser. No.		

US

1996-602228, filed on 15 Feb 1996 which is a continuation-in-part of Ser. No. US 1995-533901, filed on 26 Sep 1995 which is a continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kim, John
LEGAL REPRESENTATIVE: Sprunger, Suzanne A., Brown, Scott A.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s) ; 8 Drawing Page(s)
LINE COUNT: 2435

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making

TNF-R1-2D ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 22 OF 42 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999357922 MEDLINE
DOCUMENT NUMBER: 99357922 PubMed ID: 10427145
TITLE: Inhibition of insulin-like growth factor I receptor signaling by the vitamin D analogue EB1089 in MCF-7 breast cancer cells: A role for insulin-like growth factor binding proteins.
AUTHOR: Rozen F; Pollak M
CORPORATE SOURCE: Lady Davis Institute for Medical Research of the Jewish General Hospital and Departments of Medicine and Oncology, McGill University, Montreal, Quebec H3T 1E2, Canada.
SOURCE: INTERNATIONAL JOURNAL OF ONCOLOGY, 1999 Sep; 15 (3) 549-54.
PUB. COUNTRY: Greece
Journal code: CX5; 9908042. ISSN: 1019-6439.
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STM: 19991026
Last Updated on STM: 20000303
Entered Medline: 19991014

AB Insulin-like growth factors I and II (IGF-I and IGF-II) are potent mitogens involved in growth regulation of breast epithelial cells and are implicated in the pathophysiology of breast cancer. Their bioactivity is enhanced or inhibited by specific IGF-binding proteins (IGFBPs). Vitamin D-related compounds (VDRs) have been shown to inhibit proliferation and induce apoptosis of MCF-7 breast carcinoma cells. We have previously demonstrated that VDRs antagonize the growth-promoting activity of IGF-I by stimulating autocrine production of **IGFBP-5** in MCF-7 cells, but the effect of VDRs on IGF-I receptor (IGF-IR) intracellular signaling has not been elucidated. We report here that the vitamin D analogue EB1089 interferes with the IGF-IR signaling pathway by attenuating IGF-I-induced tyrosine phosphorylation of IRS-1, and to a lesser extent, IRS-2. It does not affect protein levels of IRS-1, IRS-2 or IGF-IR. However, EB1089 does not inhibit tyrosine phosphorylation of IRS-1 induced by des(1-3) IGF-I, an IGF-I analogue with greatly reduced affinity for IGFBPs. Furthermore, we demonstrate that an **antisense IGFBP-5** oligodeoxynucleotide attenuates EB1089-induced inhibition of IGF-I-stimulated tyrosine phosphorylation of IRS-1 and EB1089-induced **IGFBP-5** accumulation. These data strongly suggest that **IGFBP-5** plays a functional role in the interfering action of EB1089 with the IGF-IR signal transduction pathway.

L3 ANSWER 23 OF 42 USPATFULL
ACCESSION NUMBER: 1998:160103 USPATFULL
TITLE: TNF receptor death ligand proteins and inhibitors of ligand binding
INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schwella, Andre R., Winchester, MA, United States

(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5852173		19981222
APPLICATION INFO.:	US 1995-531901		19950926 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now		

abandoned

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Walsh, Stephen
ASSISTANT EXAMINER:	Kaufman, Claire M.
LEGAL REPRESENTATIVE:	Spranger, Suzanne A., Brown, Scott A., DesRosier, Thomas J.

NUMBER OF CLAIMS:	7
EXEMPLARY CLAIM:	7
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT:	1855

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing

the

TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

LE ANSWER 24 OF 42 USFATFULL

ACCESSION NUMBER:	1998:157114 USFATFULL
TITLE:	TNF receptor death domain ligand proteins and method to
	identify inhibitors of ligand binding
INVENTOR(S):	Lin, Lin-Ling, Concord, MA, United States Chen, Jennifer, Chestnut Hill, MA, United States Schievella, Andrea R., Winchester, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5849501		19981215
APPLICATION INFO.:	US 1995-494440		19950619 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Walsh, Stephen
ASSISTANT EXAMINER:	Kaufman, Claire M.
LEGAL REPRESENTATIVE:	Brown, Scott A., Spranger, Suzanne A., DesRosier, Thomas J.

NUMBER OF CLAIMS:	6
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT:	1627

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are

TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 25 OF 42 USPATEFULL

ACCESSION NUMBER: 1998:154394 USPATEFULL
TITLE: TNF receptor death domain ligand proteins
INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5847099		19981208
APPLICATION INFO.:	US 1996-640341		19960517 (3)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Walsh, Stephen		
ASSISTANT EXAMINER:	Kaufman, Claire M.		
LEGAL REPRESENTATIVE:	Brown, Scott A., DesRosier, Thomas J.		
NUMBER OF CLAIMS:	15		
EXEMPLAR CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 1 Drawing Page(s)		
LINE COUNT:	1840		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing the TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed. Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 26 OF 42 USPATEFULL

ACCESSION NUMBER: 1998:150690 USPATEFULL
TITLE: TNF receptor death domain ligand proteins and inhibitors of ligand binding
INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schievella, Andrea R., Winchester, MA, United States
Braham, James, Somerville, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5841675		19981201
APPLICATION INFO.:	US 1996-601228		19960215 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-533901, filed on 26 Sep 1995 which is a continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed		

FILE SEGMENT: Granted
PRIMARY EXAMINER: Ulm, John
LEGAL REPRESENTATIVE: Springer, Suzanne A., Brown, Scott A.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1115

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing the TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.
Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 27 OF 42 USPTFULL

ACCESSION NUMBER: 1998:49043 USPATEFULL
TITLE: Methods and reagents for the identification and regulation of senescence-related genes
INVENTORS : Linskens, Maarten H. H., Palo Alto, CA, United States
Hirsch, Kenneth S., Palo Alto, CA, United States
Villeponteau, Bryant, San Carlos, CA, United States
Feng, Junli, San Carlos, CA, United States
Punk, Walter, Union City, CA, United States
West, Michael David, Belmont, CA, United States
PATENT ASSIGNEE(S): Genen Corporation, Menlo Park, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5744300		19980423
APPLICATION INFO.:	US 1994-231420		19941031 (8)
RELATEI APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-235180, filed on 29 Apr 1994, now patented, Pat. No. US 5580726 And Ser. No. US 1994-38766, filed on 24 Mar 1993, now patented, Pat. No. US 5489503		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Myers, Carla J.		
LEGAL REPRESENTATIVE:	Kaster, KevinLynch & Lynch LLP		
NUMBER OF CLAIMS:	17		
EXEMPLARY CLAIM:	1		
LINE COUNT:	2406		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Identification of senescence-related genes can be accomplished by comparing mRNA expression between young and senescent cells. Probes complementary to such genes can be used to detect senescent cells and distinguish between young and senescent cells as well as in screens to identify compound that alter expression levels of senescence-related genes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 28 OF 42 USPTFULL

ACCESSION NUMBER: 1998:9502 USPATEFULL
TITLE: MALT, a TNF receptor death domain ligand protein
INVENTOR(S): Lin, Li-hing, Concord, MA, United States
Lin, Li-hing, Concord, MA, United States

PATENT ASSIGNEE(S):

Genetics Institute, Inc., Cambridge, MA, United States
(a corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5712381		19980127
APPLICATION INFO.:	US 1996-044551		19960815 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-602228, filed on 15 Feb 1996 which is a continuation-in-part of Ser. No. US 1995-533901, filed on 26 Sep 1995 which is a continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now		

abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Walsh, Stephen
ASSISTANT EXAMINER: Fanjan, Mukul
LEGAL REPRESENTATIVE: Brown, Scott A., Sprunger, Suzanne A., DesRosier, Thomas J.

NUMBER OF CLAIMS: 14
EXEMPLIFY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1329

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing the TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed. Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 29 OF 42 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1998187774 MEDLINE
DOCUMENT NUMBER: 98187774 PubMed ID: 9528925
TITLE: Up-regulation of **insulin-like growth factor binding protein-5** is independent of muscle cell differentiation, sensitive to rapamycin, but insensitive to wortmannin and LY294002.
AUTHOR: Rousse S; Montarras D; Pinset C; Duhais C
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale, U.142, Hopital Saint Antoine, Paris, France.
SOURCE: ENDOCRINOLOGY, (1998 Apr) 139 (4) 1487-93.
Journal code: EG2; 137040. ISSN: 0013-7227.
PUB. COUNTRY: United States
Journal: Article; JOURNAL ARTICLES
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980412
Last Updated on STN: 20000308
Entered Medline: 19980414

AB Skeletal myoblast differentiation is stimulated by insulin-like growth factors (IGFs). The autocrine action of IGFs is mediated through the type-1 IGF receptor (IGF-R1) and modulated by IGF binding proteins (IGFBPs). We have shown that the type-1 IGF receptor is expressed by the myoblast cell line stably

cells: high levels of IGFBP-2 messenger RNA (mRNA) were found only in proliferating myoblasts, whereas IGFBP-3 mRNA was induced in quiescent cells. Secretion of IGF-1 was strongly stimulated during differentiation. Insulin and IGF dose-response experiments showed that up-regulation of IGFBP-5 resulted from IGF-1 activation. Drugs interfering with IGF-1 signaling and inhibiting myoblast differentiation had different effects on IGFBP-5 up-regulation. Two phosphatidylinositol 3-kinase (PI 3-kinase) inhibitors, wortmannin and LY294002 [2-(4-morpholinyl)-8-phenyl-4H-1-benzopyran-4-one], failed to alter IGFBP-5 up-regulation, which persisted in the absence of differentiation. Rapamycin which indirectly prevents activation of the p70 ribosomal protein-S6 kinase (p70S6k), suppressed IGFBP-5 induction. Because the PI3-kinase inhibitors block p70S6k, neither kinase would be required for IGF-1 dependent IGFBP-5 induction. In C2 anti-IGF-II myoblasts, IGFBP-5 induction is therefore rapamycin-sensitive and independent of differentiation.

13 ANSWER 30 OF 42 MEDLINE DUPLICATE 7
 ACCESSION NUMBER: 1999095111 MEDLINE
 DOCUMENT NUMBER: 99095111 PubMed ID: 9879061
 TITLE: Differential expression and localization of IGF-I and IGF binding proteins in inflamed rat colon.
 AUTHOR: Zeen J M; Mohapatra M; Lund P K; Eysselein V E; McRoberts J
 CORPORATE SOURCE: A
 Harkin-UCLA Medical Center, Division of Gastroenterology, Torrance, CA, USA.
 CONTRACT NUMBER: DK34597 (NIDDK)
 DK42874 (NIDDK)
 DK47769 (NIDDK)
 SOURCE: JOURNAL OF RECEPTOR AND SIGNAL TRANSDUCTION RESEARCH, (1995)
 Jul-Nov) 13 (4-6) 265-80.
 Journal code: CCU; 9909432. ISSN: 1079-9893.
 PUB. COUNTRY: United States
 Journal: Article: (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199903
 ENTRY DATE: Entered STN: 19990326
 Last Updated on STN: 19990326
 Entered Medline: 19990313
 AB Recent studies indicate increased insulin-like growth factor I (IGF-I) expression and altered expression of IGF binding proteins (IGFBP) in the bowel during experimental colitis. This study analyzes the cellular sites of altered IGF-I and IGFBP-expression in large bowel of rats with experimental colitis. Colitis was induced by colonic instillation of 2, 4, 6-trinitrobenzenesulfonic (TNE) acid in ethanol. Animals were sacrificed at 7 days after induction of colitis. Cryostat sections of colon from TNE-treated and control rats were hybridized with 32S-labeled antisense probes for IGF-I, IGFBP-3, IGFBP-4 and IGFBP-5. IGF I mRNA was up-regulated in lamina propria cells, submucosa and smooth muscle of inflamed colon. IGFBP-3 mRNA was localized to lamina propria and was down-regulated in inflamed colon. IGFBP-4 and IGFBP-5 mRNAs were both up-regulated in inflamed colon. IGFBP-4 mRNA was increased in lamina propria, submucosa and smooth muscle, whereas IGFBP-5 mRNA was increased in smooth muscle. Increased IGF-I expression in mesenchymal layers of colon during experimental colitis supports the hypothesis that IGF-I contributes to the pathogenesis of inflammatory bowel disease. Altered expression

action.

13 ANSWER 31 OF 42 MEDLINE
ACCESSION NUMBER: 97278358 MEDLINE
DOCUMENT NUMBER: 97278358 PubMed ID: 9133435
TITLE: Insulin-like growth factor binding protein gene expression in the pregnant rat uterus and placenta.
AUTHOR: Cerro J A; Fintar J E
CORPORATE SOURCE: Department of Anatomy and Cell Biology, Columbia University
College of Physicians and Surgeons, New York, New York 10032, USA.
CONTRACT NUMBER: NS21970 (NINDS)
SOURCE: DEVELOPMENTAL BIOLOGY, (1997 Apr 15) 184 (2) 278-95.
Journal code: E7T; 0872762. ISSN: 0012-1636.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19970612
Entered Medline: 19970602

AB While the insulin-like growth factor (IGF) system plays a fundamental role in regulating embryonic and placental growth, the specific contributions of the six IGF binding proteins (IGFBPs 1-6) to these processes are not well understood. We here focus on IGFBP expression in the extraembryonic environment, which both supports and constrains embryonic growth, and have used in situ hybridization to determine sites of IGFBP mRNA synthesis in the pregnant rat uterus and placenta. We find that all IGFBPs are expressed in distinct, changing patterns in the uterine endometrium, at the decidual boundary, in the decidual vasculature, and in the myometrium during pregnancy. Within the endometrium, the most prominent change is that expression of IGFBP-1 begins in some, but not all, endometrial glands prior to implantation and then expands to include all secretory epithelia shortly after implantation. During the period of rapid decidual proliferation that follows implantation, IGFBP-3, -4, and -5 transcripts are all detected in a laminar array at the boundary between the decidua and the nondecidualized endometrium. In the decidual vasculature at Day (d) 8.0, both IGFBP-3 and IGFBP-4 mRNAs are detected in dilating blood vessels, with BP-3 most prominent in the antimesometrial plexus and BP-4 primarily at the mesometrial pole. Later (d11.5), all decidual vessels express high levels of IGFBP-3 and lower levels of IGFBP-4 mRNAs. Finally, changes in expression of several IGFBPs also occur within the myometrium during pregnancy. For example, IGFBP-2 is expressed in the inner circular layer shortly after implantation, and expression increases through late gestation. In contrast, **IGFBP-5** hybridization occurs over both myometrial layers before implantation, but decreases in intensity and spatial distribution as pregnancy proceeds. Finally, and most strikingly, IGFBP-6 expression, barely detectable in the d7.0 myometrium, gradually increases until it is very strongly transcribed during the placental stages. Taken together, these observations suggest multiple roles for IGFBPs in supporting implantation, regulating the extent of decidualization, modulating local levels of vascular IGFs, and regulating uterine muscular growth.

14 ANSWER 32 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:372963 BIOSIS
DOCUMENT NUMBER: PREV199799672196
To cite this study on the role of insulin-like

AUTHOR(S): Kanzaki, S. (1); Mohan, S.; Ono, T. (1); Matsusaka, Y. (1);
Moriwaka, T. (1); Tanaka, H. (1); Seino, Y. (1)
CORPORATE SOURCE: (1) Dep. Pediatrics, Okayama Univ. Med. Sch., Okayama 700
Japan
SOURCE: Hormone Research (Basel), (1997) Vol. 48, No. SUPPL. 2,
p5.
16.
Meeting Info.: 5th Joint Meeting of the European Society
for Paediatric Endocrinology and the Lawson Wilkins
Society
for Pediatric Endocrinology, in Collaboration with the
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Australian Paediatric Endocrine Group, the Japanese
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for Paediatric Endocrinology Stockholm, Sweden June 22-26,
1997
ISSN: 0301-0163.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

LE ANSWER 33 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:211809 CAPLUS

DOCUMENT NUMBER: 124:270541

TITLE: Use of **antisense** nucleic acids/analog
inhibiting growth factor-mediated cell proliferation
for treatment of proliferative and/or inflammatory
skin disorders

INVENTOR(S): Wertner, George Arthur; Wraight, Christopher John

PATENT ASSIGNEE(S): Royal Children's Hospital Research Foundation,
Australia

SOURCE: PCT Int. Appl., 119 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9601636	A1	19960105	WO 1995-AU410	19950706
W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, PQ, RU, SD, SE, SG, SI, SK, TJ, TM, TT			
RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BG, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2194366	AA	19960105	CA 1995-2194366	19950706
AU 9523753	A1	19960109	AU 1995-23753	19950706
AU 952378	B2	19980604		
EP 776210	A1	19970604	EP 1995-924110	19950706
E:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			
JP 508246	T2	1999-018	JP 1995-504113	19950706
US 582904	A	1999-027	US 1995-504113	19950706
US 584741	B1	20010104	US 1995-150926	19951126

PRIORITY APPLN. INFO.:

AU 1994-6723	A	19940706
WO 1995-AU410	W	19950706
US 1996-666392	A1	19960820

AB The present invention relates generally to a method for the prophylaxis and/or treatment of skin disorders, and in particular proliferative and/or

inflammatory skin disorders, and to nucleic acids or nucleic acid analogs

stimulation of this layer of cells. The present invention contemplates, in a most preferred embodiment, a method for the prophylaxis and/or treatment of psoriasis. Phosphorothioate-linked oligonucleotide (18- and 24-mers) **antisense** to human insulin-like growth factor binding protein 3-encoding nucleic acid inhibited IGFBP-3 synthesis by HaCat cells (human differentiated keratinocyte cell line).

L3 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1996:254613 CAPLUS
DOCUMENT NUMBER: 124:308419
TITLE: Osteogenic protein-1-mediated insulin-like growth factor gene expression in primary cultures of rat osteoblastic cells
AUTHOR(S): Ren, Lee-Chuan C.; Adams, Martin L.; Kitten, Allison M.; Olson, Merle S.; Lee, John C.
CORPORATE SOURCE: Department Biochemistry, University Texas Health Science Center, San Antonio, TX, 78284-7760, USA
SOURCE: Endocrinology (1996), 137(5), 1911-11
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Osteogenic protein-1 (OP-1) is a member of the bone morphogenetic protein family and has been shown to induce new bone formation in vivo. In the present study, the authors detd. whether the expression of the IGF system,

a significant growth factor system in bone, was altered by OP-1 in primary cultures of fetal rats calvarial cells. Levels of mRNA encoding insulin-like growth factor I (IGF-I, IGF-II, IGF-I receptor, and IGF-binding proteins (IGFBP-1) mRNA was elevated in an OP-1 concn. (0-1000 ng/mL)-dependent manner, with maximal stimulation of IGF-I mRNA

of 2- to 3-fold apparent 24 h after treatment. The increase in the IGF-I mRNA level involved a preferential stimulation of transcripts initiated at

start site 2 in the exon 1 promoter. The level of IGF-II mRNA also increased by approx. 2-fold in OP-1-treated cells in a concn.-dependent manner. The level of IGF-I receptor mRNA was not altered by treatment. Whereas IGFBP-1 mRNA was not detected in these cells, IGFBP-2 mRNA was expressed, but the expression was not changed after treatment for 48 h in the concn. range (0-1000 ng/mL) tested. The IGFBP-2 mRNA level was increased slightly 48 h after OP-1 treatment in a concn.-dependent manner.

The IGFBP-4, -5, and -6 mRNA levels decreased dramatically in an OP-1 concn.-dependent manner. In addn., incubation of **antisense** oligonucleotides corresponding to IGF-I or -II mRNA sequence with OP-1 reduced the OP-1-induced elevation in alk. phosphatase activity. The present results suggest that the differentiation of rat osteoblastic cells

in response to OP-1 is mediated in part by increased IGF-I and -II gene expression and alterations in the gene expression of different IGFBPs.

L1 ANSWER 35 OF 42 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 97084055 MEDLINE
DOCUMENT NUMBER: 97084055 PubMed ID: 8930399
TITLE: A role for insulin-like growth factor binding protein 5 in the antiproliferative action of the antiestrogen ICI 162730.
AUTHOR: Huynh H; Yang X F; Pollak M
CORPORATE SOURCE: Lady Davis Research Institute, Jewish General Hospital, Montreal, Quebec, Canada.
SOURCE: CELL GROWTH AND DIFFERENTIATION, 1996 Nov 7; 7(11):1511-6.

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970227

AB Insulin-like growth factors (IGFs) are potent mitogens for breast cancer cells. Although IGF-binding proteins (IGFBPs) are known to regulate access

of IGFs to IGF receptors, their precise biological actions are poorly defined. We observed that the potent antiestrogen ICI 162780 (ICI) increased **IGFBP-5** mRNA by 2- to 3-fold in 3,10-dimethyl-1,2-benzanthracene-induced mammary tumors in vivo. In vitro studies showed that growth inhibition of MCF-7 human breast cancer cells induced by ICI was associated with increased transcription of the **IGFBP-5** gene, increased **IGFBP-5** mRNA abundance, and increased **IGFBP-5** protein accumulation in the conditioned medium. Growth stimulation following estradiol

exposure

was associated with opposite effects. An **IGFBP-5 antisense** oligodeoxynucleotide significantly decreased **IGFBP-5** accumulation in conditioned media and enhanced MCF-7 cell DNA synthesis. Furthermore, this **antisense** oligodeoxynucleotide attenuated both antiestrogen-induced **IGFBP-5** accumulation and antiestrogen-induced growth inhibition. These data demonstrate that estradiol down-regulates and ICI up-regulates an autocrine **IGFBP-5** growth inhibitory pathway in MCF-7 cells and suggest that **IGFBP-5** plays a role in modulation of proliferation of breast cancers by estrogens and antiestrogens.

L3 ANSWER 36 OF 42 MEDLINE DUPLICATE 10

ACCESSION NUMBER: 96245121 MEDLINE
DOCUMENT NUMBER: 96245221 PubMed ID: 8641849
TITLE: Localization of mRNAs for insulin-like growth factor-I (IGF-I), IGF-I receptor, and IGF binding proteins in rat eye.
AUTHOR: Burrin C F; Berka J L; Edmondson S R; Werther G A; Batch J A
CORPORATE SOURCE: Centre for Hormone Research, Royal Children's Hospital, Parkville, Victoria, Australia.
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1996 Jun) 37 (7): 1459-68.
JOURNAL CODE: GWI; 7709711. ISSN: 0146-0404.
PUB. COUNTRY: United States
JOURNAL; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960726
Last Updated on STN: 20000302
Entered Medline: 19960718

AB PURPOSE. To localize mRNA for insulin-like growth factor (IGF)-I, IGF-I receptor (IGF-IR), and IGF binding protein (BP) 1 to IGFBP-6 in the rat eye. METHODS. cDNA sequences for IGF-I, IGF-IR, and IGFBP-1 to IGFBP-6 were used to synthesize 3'-S-CTP labeled **antisense** and sense probes for in situ hybridization on 5-microns sections of the rat eye, including the retina, choroid, sclera, ciliary body, and cornea. RESULTS. IGF-I mRNA was demonstrated over ganglion cells of the retina and endothelial cells of the choroid and ciliary processes. IGF-IR mRNA showed

more extensive distribution, localizing to the retinal ganglion cell layer, ciliary body, and endothelial cells of the choroid and also the

and lens. IGFBP-1 mRNA localized to outer nonpigmented epithelia of the ciliary processes and the germinal layer of corneal epithelium as well as iris, conjunctiva, and sclera. Messenger RNAs for IGFBP-1 to IGFBP-6 localized to choroidal endothelial cells and chromatophores and also to the inner pigmented epithelium of the ciliary processes. Messenger RNAs for **IGFBP-5** and IGFBP-6 were seen in the inner and outer nuclear layers of the neural retina. IGFBP-1 mRNA was not detected within the rat eye. **CONCLUSIONS.** Using in situ hybridization, we have demonstrated mRNAs for IGF-I, IGF-II, and IGFBP-1 to IGFBP-6 in specific histologic layers of the retina, choroid, ciliary body, and cornea in the rat. The characterization of the IGF system in vivo suggests specific roles in the normal eye and provides a basis for studying the IGF system in eye pathology.

13 ANSWER 37 OF 42 MEDLINE DUPLICATE 11

ACCESSION NUMBER: 96223370 MEDLINE
DOCUMENT NUMBER: 96223370 PubMed ID: 8686241
TITLE:

Insulin-like growth factor binding protein-5

5 modulates muscle differentiation through an insulin-like growth factor-dependent mechanism.

AUTHOR: James L L; Stewart C E; Rotwein P
CORPORATE SOURCE: Department of Biochemistry, Washington University, School of Medicine, St. Louis, Missouri 63110, USA.
CONTRACT NUMBER: BRJ1 DP42748 (NIDDK)
DEK0579 (NIDDK)
SOURCE: JOURNAL OF CELL BIOLOGY, (1996 May) 133 (3) 683-93.
Journal code: HMV; 0371356. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal: Article: JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960719
Last Updated on STN: 19960719
Entered Medline: 19960711

AB The insulin-like growth factor binding proteins (IGFBPs) are a family of six secreted proteins which bind to and modulate the actions of insulin-like growth factors-I and -II (IGF-I and -II). **IGFBP-5** is more conserved than other IGFBPs characterized to date, and is expressed in adult rodent muscle and in the developing myotome. We have

shown previously that C2 myoblasts secrete **IGFBP-5** as their sole IGFBP. Here we use these cells to study the function of **IGFBP-5** during myogenesis, a process stimulated by IGFs. We stably transfected C2 cells with **IGFBP-5** cDNAs under control of a constitutively active promoter. Compared with vector-transfected control cells, C2 myoblasts expressing the **IGFBP-5** transgene in the sense orientation exhibit increased **IGFBP-5** levels in the extracellular matrix during proliferation, and subsequently fail to differentiate normally, as assessed by both morphological and biochemical criteria. Compared to controls, **IGFBP-5** sense myoblasts show enhanced survival in low serum medium, remaining viable for at least four weeks in culture. By contrast, myoblasts expressing the **IGFBP 5 antisense** transcript differentiate prematurely and more extensively than control cells. The inhibition of myogenic differentiation

by high level expression of **IGFBP-5** could be overcome by exogenous IGFs, with des (1-3) IGF-I, an analogue with decreased affinity for **IGFBP-5** but normal affinity for the IGF-I receptor, showing the highest potency. These results are consistent with

model in which **IGFBP-5** blocks IGF-stimulated

suggest that **IGFBP-5** normally inhibits muscle differentiation, and may play a role for **IGFBP-5** in regulating IGF action during myogenic development in vivo.

13 ANSWER 39 OF 42 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 87052388 MEDLINE
DOCUMENT NUMBER: 87052388 PubMed ID: 8897022
TITLE: Growth hormone and the insulin-like growth factor system
is myogenesis.
AUTHOR: Florini J R; Ewton D Z;apolican S A
CORPORATE SOURCE: Biology Department, Syracuse University, New York 13244,
USA.
CONTRACT NUMBER: HL11551 (NHLBI)
SOURCE: ENDOCRINE REVIEWS, (1996 Oct) 17 (5) 491-517. Ref: 465
Journal code: EIK; 8806258. ISSN: 0163-769X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 19970227
Entered Medline: 19970211

AB It is very clear that the GH-IGF axis plays a major role in controlling the growth and differentiation of skeletal muscles, as it does virtually all of the tissues in the animal body. One aspect of this control is unquestioned: circulating GH acts on the liver to stimulate expression of the IGF-I and IGFBP3 genes, substantially increasing the levels of these proteins in the circulation. It also seems that GH stimulates expression of IGF-I genes in skeletal muscle, although there are a number of cases in which skeletal muscle IGF-I expression is elevated in the absence of GH. It is substantially less clear that GH acts directly on skeletal muscle to stimulate its growth; the presence of GH receptor mRNA in skeletal muscle is well established, but most investigators have been unsuccessful in demonstrating any specific binding of GH to skeletal muscle or to myoblasts in culture. It has been equally difficult to show direct actions of GH on cultured muscle cells; the only positive report concludes that the early insulin-like effects of GH can result from direct interactions between GH and isolated muscle cells. The effects of the IGFs on skeletal muscle are much clearer. It is well established by studies in a number of laboratories on a variety of systems that IGFs stimulate many anabolic responses in myoblasts, as they do in other cell types. IGFs have the unusual property of stimulating both proliferation and differentiation of myoblasts, responses that are generally believed to be mutually exclusive: in myoblasts, they are in fact temporally separated. The stimulation of differentiation by IGF-I is (at least in part) a result of substantially increased levels of the mRNA for myogenin, the member of the MyoD family most directly associated with terminal myogenesis. As levels of myogenin mRNA rise, those of myf-5 mRNA (the only other member of the MyoD family expressed significantly in L6 myoblasts) fall dramatically, although myf-5 expression is required for the initial elevation of myogenin. The effects of IGFs are significantly modulated by IGFBPs secreted by myoblasts in serum-free medium, inhibitory IGFBPs-4 and -6 are expressed and secreted by L6A1 myoblasts, while expression of **IGFBP-5** rises dramatically as differentiation proceeds. Other myoblasts also secrete IGFBP-2. Even if exogenous IGFs are not added to the low-serum

myogenic cell lines, (such as Sol 8) are so active in expressing the IGF-II gene that it is not possible to demonstrate effects of exogenous IGFs. This autocrine expression of IGFs is by no means unique to skeletal muscle cells; indeed, it is so widely seen in cells responding to mitogenic stimuli that we suggest that IGFs can be viewed as extracellular

second messengers that mediate most, if not all, such actions of agents that stimulate cell proliferation. The component of serum that suppresses IGF-II gene expression under "growth" conditions appears to be the IGFs themselves, which exhibit a very high potency in the feedback inhibition of IGF-II expression. In addition, IGFs have effects on the expression of other genes related to differentiation. Treatment of L6A1 cell with IGFs suppresses their expression of the myogenesis-inhibiting TGF beta s with

a time course consistent with an initial proliferative step followed by differentiation, i.e. expression is first increased and then very substantially decreased. It is not established that this plays a role in control of differentiation, but experiments with EGF **antisense** constructs suggests that this may well be the case. Until recently, IGFs were the only circulating agents known to stimulate myoblast differentiation, in contrast to the relatively large number of growth factors that inhibit the process. It is now clear that thyroid hormones and RA also stimulate myogenesis, and that IL-1 β enhances the stimulatory eff

L3 ANSWER 39 OF 41 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 96109186 MEDLINE
DOCUMENT NUMBER: 96109186 PubMed ID: 9613825
TITLE: Insulin-like growth factor II mediates epidermal growth factor-induced mitogenesis in cervical cancer cells.
AUTHOR: Steller M A; Delgado C H; Zou Z
CORPORATE SOURCE: Section of Gynecologic Oncology, National Cancer Institute,
Bethesda, MD 20892-1502, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Dec 19) 92 (26) 11970-4.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960620
Last Updated on STN: 20000303
Entered Medline: 19960607

AB There is increasing evidence that activation of the insulin-like growth factor I (IGF-I) receptor plays a major role in the control of cellular proliferation of many cell types. We studied the mitogenic effects of IGF-I, IGF-II, and epidermal growth factor (EGF) on growth-arrested HT-3 cells, a human cervical cancer cell line. All three growth factors promoted dose-dependent increases in cell proliferation. In untransformed cells, EGF usually requires stimulation by a "progression" factor such as IGF I, IGF II, or insulin (in supraphysiologic concentrations) in order

to exert a mitogenic effect. Accordingly, we investigated whether an autocrine pathway involving IGF I or IGF-II participated in the EGF-induced mitogenesis of HT-3 cells. With the RNase protection assay, IGF-I mRNA was not detected. However, IGF-II mRNA increased in a time-dependent manner following EGF stimulation. The EGF-induced mitogenesis was abrogated in a dose-dependent manner by IGF-binding protein 5 (IGFBP-5), which binds to IGF-II and neutralizes it. An **antisense** oligonucleotide to IGF-II also inhibited the proliferative response to EGF. In addition, prolonged, but not short-term, stimulation with EGF resulted in autophosphorylation of

secretion of IGF-II in HT-3 cervical cancer cells can participate in EGF-induced mitogenesis and suggest that autocrine signals involving the IGF-I receptor occur "downstream" of competence growth factor receptors such as the EGF receptor.

LS ANSWER 40 OF 42 MEDLINE DUPLICATE 14
 ACCESSION NUMBER: 96082466 MEDLINE
 DOCUMENT NUMBER: 96082466 PubMed ID: 7474972
 TITLE: Regulation of insulin-like growth factor (IGF)-binding protein-6 and mannose 6-phosphate/IGF-II receptor expression in IGF-II-overexpressing NIH 3T3 cells.
 AUTHOR: Claussen M; Buerigisser D; Schaller A G; Matzner U; Bräulke T
 CORPORATE SOURCE: Institute for Biochemistry II, University of Göttingen, Germany.
 SOURCE: MOLECULAR ENDOCRINOLOGY, (1996 Jul) 9 (7) 902-12.
 Journal code: M32; 8801431. ISSN: 0888-8809.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199512
 ENTRY DATE: Entered STM: 19960124
 Last Updated on STM: 20001303
 Entered Medline: 19951212

AB Insulin-like growth factor II (IGF-II)-overexpressing NIH 3T3 cells were used to examine regulation of insulin-like growth factor binding protein (IGFBP) and mannose 6-phosphate (M6P)/IGF-II receptor expression. Ligand blot analysis of conditioned media indicated a predominant IGFBP of 26-28 kilodaltons the abundance of which is 3- to 10-fold higher in media of IGF-II-overexpressing cells. The IGFBP level in control cell medium was increased by incubation in the presence of IGF-II, IGF-I, and mutant IGF-II forms with reduced affinities for IGF-I or M6P/IGF-II receptors. Further proof that IGF-II regulated the IGFBP was obtained by incubation of IGF-II overexpressing cells in the presence of **antisense** IGF-II oligomers or anti-IGF-II antibodies, which resulted in significant reduction of the IGFBP in conditioned medium. Mouse IGFBP-6 mRNA expression was increased in IGF-II-overexpressing or IGF-II-treated control cells. The IGFBP contained O-linked carbohydrate residues and was recognized by an antiserum to rat IGFBP-6. To determine whether IGFs were influencing proteolytic degradation of IGFBPs, cell-free conditioned

media were incubated at 37 C with recombinant human IGFBPs. At neutral pH proteolysis of **IGFBP-5** occurred during incubation in conditioned media from control and IGF-II-overexpressing cells. Upon acidification of the medium samples, only the degradation of IGFBP-6 was prevented in IGF-II-overexpressing cell-conditioned medium. (ABSTRACT TRUNCATED AT 250 WORDS)

LS ANSWER 41 OF 42 MEDLINE DUPLICATE 15
 ACCESSION NUMBER: 94259769 MEDLINE
 DOCUMENT NUMBER: 94259769 PubMed ID: 9515389
 TITLE: Expression of the genes encoding the insulin-like growth factors (IGF-I and II), the IGF and insulin receptors, and IGF binding proteins-1-6 and the localization of their gene products in normal and polycystic ovary syndrome ovaries.
 AUTHOR: el-Resky A; Chen X; Roberts V J; Shimazaki S; Ling N; LeRoith D; Roberts J T Jr; Yen S S
 CORPORATE SOURCE: Department of Reproductive Medicine, University of California School of Medicine, La Jolla 92093.
 CONTRACT NUMBER: HD-07203-10 (NICHD)
 HD-07213-11 (NICHD)
 HD-07213-12 (NICHD)

JOURNAL CODE: HRB; 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
JOURNAL: Article; JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940714
Last Updated on STN: 20000303
Entered Medline: 19940705

AB To discern the potential role of the insulin-like growth factors (IGFs)
in

polycystic ovary syndrome (PCOS), we examined the expression of the genes encoding the IGFs, IGF receptors (IGFr), insulin receptor (Ir), and IGF-binding proteins (IGFBPs-1-6) as well as the localization of the gene products in specific cellular compartments of normal and PCOS human ovaries. Messenger ribonucleic acid (mRNA) was localized by in situ hybridization with specific 35S-labeled human **antisense** RNA probes, and protein was detected by immunohistochemistry using specific antisera. Thecal cells, but not granulosa cells (GC), of small antral follicles (3-6 mm) from PCOS ovaries expressed both IGF-1 and IGF-11 transcripts. Abundant IGF-1r mRNA was found only in GC, IGF-11r mRNA was found in both granulosa and thecal cells, and Ir mRNA was detected in all cell types, including granulosa, thecal, and stromal cells. Localization of the gene products revealed no IGF-1 immunoreactivity; however, immunostaining for each of the other gene products was colocalized with its corresponding mRNA. The cellular distribution of mRNA and protein in PCOS follicles was indistinguishable from that observed in small antral follicles from normal ovaries. In dominant follicles, however, IGF-1 mRNA was no longer detectable, but abundant IGF-11 mRNA was expressed exclusively in GC. Although IGF-1r mRNA was expressed in GC, IGF-11r mRNA was found in both granulosa and thecal cells. In follicles taken from

PCOS ovaries, no IGFBP-1 mRNA was detected, IGFBP-2 mRNA was abundant in both granulosa and thecal cells, moderate IGFBP-3 mRNA was found only in thecal

cells, IGFBP-4 and -5 mRNAs were present in all cellular compartments, and

IGFBP-6 mRNA was not detected. Localization of the gene products by immunostaining revealed that each protein colocalized with its corresponding mRNA. The cellular distribution of IGFBP mRNA and protein

in PCOS follicles was also indistinguishable from that in small antral follicles of normal ovaries, but remarkable differences were found in dominant follicles, where abundant IGFBP-1 mRNA was seen exclusively in GC, IGFBP-2 mRNA in thecal cells, and IGFBP-3 mRNA in both granulosa and thecal cells. Moderate expression of the IGFBP-4 and **IGFBP-5** genes was seen in all cell types, including stromal cells, but no IGFBP-6 mRNA was detected. Again, each of the gene products colocalized

with its corresponding mRNA. We conclude the following. (ABSTRACT TRUNCATED

AT 400 WORDS)

LE ANSWER 41 OF 42 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 95151319 MEDLINE
DOCUMENT NUMBER: 95151319 PUBMED ID: 7525047
TITLE: Localization of messenger ribonucleic acid for
insulin-like growth factor-binding proteins in human skin by in situ hybridization.
AUTHOR: Batch J A; Mendiri F A; Edmondson E R; Werther G A
CORPORATE SOURCE: Center for Hormone Research, University of Melbourne, Royal
Children's Hospital, Parkville, Australia.

Journal code: HRB; 0375362. ISSN: 0021-972X.
 PUB. COUNTRY: United States
 Journal/ Article: (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 199412
 ENTRY DATE: Entered STN: 19950113
 Last Updated on SIN: 20000903
 Entered Medline: 19941221

AB The role of the insulin-like growth factors (IGFs) in human skin physiology has been increasingly recognized, although relatively little is known about the cell types involved or the cellular mechanisms that mediate these responses. Epidermal keratinocytes and dermal fibroblasts both possess IGF-I receptors and are responsive to IGF-I. IGF-binding proteins (IGFBPs), known modulators of IGF action, may also be responsible for targeting IGF-I to its receptors and are produced by both cultured keratinocytes and fibroblasts. To demonstrate sites of production of IGFBPs in human skin, we have used in situ hybridization to localize messenger ribonucleic acid (mRNA) for the six IGFBPs. **Antisense** and sense RNA probes for the IGFBPs (IGFBP-1 to -6) were produced, and 5-microns sections of normal adult human male chest skin were probed. The control probe used was keratin-5, which is known to hybridize to the basal keratinocytes of the epidermis. mRNAs for human IGFBP-2, -3, -4, and -5 were identified, with mRNAs for IGFBP-2 and IGFBP-4 localized in sebaceous glands and eccrine sweat glands (epidermal origin). IGFBP-3 mRNA in the basal layer of the epidermis and mRNAs for IGFBP-4, and **IGFBP-5** found throughout the dermis. mRNAs for IGFBP-1 and -6 were not identified in human skin. These studies demonstrate specific localization of IGFBP mRNAs in adult human skin, suggesting that each IGFBP may play a specific role in targeting IGF-I to its receptor on responsive cells and, ultimately, in modulation of IGF-I action in skin.

Word index kwic 10 12 14 15 18 22-29 31 32 33

LB ANSWER 10 OF 42 USFATFULL
 ACCESSION NUMBER: 2001:44198 USFATFULL
 TITLE: Treatment of partial growth hormone insensitivity syndrome
 INVENTOR(S): Attie, Kenneth M., San Francisco, CA, United States
 Carlsson, Lena M. S., Gothenburg, Sweden
 Gesundheit, Neil, Los Altos, CA, United States
 Goddard, Audrey, San Francisco, CA, United States
 PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States
 States
 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6,200,000	B1	20010327
APPLICATION INFO.:	US 1994-224982		19950313 LB
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-411430, filed on 24 Mar 1995, now abandoned Continuation of Ser. No. US 1994-224982, filed on 7 Apr 1994, now patented, Pat. No. US 5646113		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Jones, Lwayne J.		
ASSISTANT EXAMINER:	Delacroix-Murhead, C.		

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 44 (Drawing Figures 1-38 Drawing Pages 39-44)
LINE COUNT: 1400

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . together with any one or more of its binding proteins, for example, those currently known, i.e., IGFBP-1, IGFBP-2, IGFBP-3, IGFBP-4, **IGFBP-5**, or IGFBP-6. The IGF-I may also be coupled to a receptor or antibody or antibody fragment for administration. The preferred. . .

DETD . . . exons 4-10 including the intron-exon boundaries were individually amplified by polymerase chain reaction (PCR) using primer pairs (of which the **antisense** was biotinylated) deduced from the published DNA sequence (3) (Sequences available on request). The

PCR products were submitted to direct. . .

L3 ANSWER 11 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:424132 BIOSIS

DOCUMENT NUMBER: PREV200100424132

TITLE: The IGF/IGFBP system in CNS malignancy.

AUTHORS : Zumkeller, W. (1); Westphal, M.

CORPORATE SOURCE: (1) Department of Pediatrics, Martin-Luther-University Halle-Wittenberg, University Hospital, Ernst-Grube-Str.

40,

06097, Halle/Saale; walter.zumkeller@medizin.uni-halle.de
Germany

SOURCE: Molecular Pathology, (August, 2001) Vol. 34, No. 4, pp. 227-229, print.
ISSN: 1365-8714

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB. . . are expressed in gliomas and, in particular, the type I IGF receptor

appears to be upregulated in malignant brain tissue. **Antisense** IGF-I receptor mRNA induces an antitumour response, resulting in complete brain tumour regression. Clinical trials for the treatment of brain tumours in humans based on a gene transfer protocol using IGF-I receptor **antisense** are under way. All six IGFBPs are expressed to a variable extent in brain tumours. High concentrations of IGFBP-2 are. . .

IT . . .
disease, nervous system disease; medulloblastoma: neoplastic disease, nervous system disease; meningioma: neoplastic disease, nervous system disease

IT Chemicals & Biochemicals

antisense insulin-like growth factor-I receptor messenger RNA; insulin-like growth factor binding protein-1; insulin-like growth factor binding protein-2; insulin-like growth factor binding protein-3;

insulin-like growth factor binding protein-4; **insulin-like growth factor binding protein-5**; insulin-like growth factor binding protein-6; insulin-like growth factor-I; insulin-like growth factor II; type I insulin like growth factor receptor; type II insulin-like. . .

L3 ANSWER 14 OF 42 USPTFULL

ACCESSION NUMBER: 2000:18550 USPTFULL

TITLE: Insulin like growth factor binding protein (IGFBP-6)

INVENTOR(S): Kiefer, Michael C., Clayton, CA, United States
Masarik, Frank R., San Francisco, CA, United States
Zurfl, Jürgen Johann Leonold, Zurich, Switzerland

corporation)

NUMBER KIND DATE
PATENT INFORMATION: US 6005468 20000215
APPLICATION INFO.: US 1997-917204 19970825 (8)
RELATED APPLN. INFO.: Continuation of Ser. No. US 1990-576648, filed on 31
Aug 1990, now abandoned which is a division of Ser.
No.
US 1990-574613, filed on 28 Aug 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Carlson, Karen Cochran
LEGAL REPRESENTATIVE: Ekins & Associates, Gith, Joseph H., Blackburn,
Robert

P.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 1749

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DEWD . . . human IGFBI-4, to the known sequences of the three human
binding proteins discussed above and another new human binding protein,
IGFBP-5. Areas of homology can be seen in these
sequences. These areas of homology are of particular interest as they
indicated. . . .

DETD . . . for IGFBI-4 were: (1) a "sense" primer consisting of a mixture
of 64 27-mers [5' AGATCTGAATTGCA(A/G)GXXGTGCA(A/G)GC 3'] and (2) an "
antisense" primer consisting of a mixture of 64 28-mers [5'
ASATCTGAATTG(A/G)TC(C/T)TC(C/T)TC(C/T)TCXAC 3'] where X denotes all
four deoxynucleotides. Eco RI sites. . . .

13 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:411772 CAPLUS
DOCUMENT NUMBER: 131:68554
TITLE: Insulin-like growth factor binding protein fragments
and their use in diagnosis and therapy
INVENTOR(S): Forssmann, Wolf-Georg; Standker, Ludger; Obendorf,
Maik; Kling, Lothar; Opitz, Hans-Georg; Mostafavi,
Hossein
PATENT ASSIGNEE(S): Germany
SOURCE: ECT Int. Appl., 62 pp.
CODEN: PIXX12
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932620	A1	19990701	WO 1998-EP8405	19981222
W: CA, JP, US RW: AT, BE, CH, CY, IE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MG, NL, PT, SE				
DE 1991251	A1	19990701	DE 1998 4057055	19981222
CA 2311974	AA	19990701	CA 1998 2311974	19981222
EP 111476	A1	20001111	EP 1998 60865	19981222
E: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE, IE				
JP 2001508931	T2	20020326	JP 2000-525539	19981222
PRIORITY APPLN. INFO.: DE 1997-19757250 A 19971222 WO 1998-EP8405 W 19981222				

OTHER SOURCE(S): MARPAT 131:68554
REFERENCE COUNT: 5 THERE ARE 5 CITEL REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (to IGFBP peptide-binding nucleic acid; insulin-like growth factor
 binding protein fragments and their use in diagnosis and therapy)
 IT 220766-05-2P
 RL: BAC (Biological activity or effector, except adverse); BPR
 (Biological
 process); BSU (Biological study, unclassified); PUR (Purification or
 recovery); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); PROC (Process); USES (Uses)
 IGFBP-5 fragment; insulin-like growth factor
 binding protein fragments and their use in diagnosis and therapy)

LE ANSWER 18 OF 42 CAPLUS COPYRIGHT 2000 ASS

ACCESSION NUMBER: 1999:03627 CAPLUS
 DOCUMENT NUMBER: 1:1:341964
 TITLE: Compositions and methods for extending the action of
 clostridial neurotoxin and modulating neurite
 outgrowth in damaged neural endplates
 INVENTOR(S): Dolly, J. Oliver; Ack1, Kai Roger; De Paiva, Anton
 PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
 SOURCE: PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY APP. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953399	A1	19991104	WO 1999-US8303	19990415
W: AL, AM, AT, AU, AC, BA, BE, BG, BF, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GL, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TC, TM, TR, TT, UA, US, UG, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,				
TM				
RW: GH, GM, KE, LS, MW, SE, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MF, NE, SN, TD, TG				
AU 9937484	A1	19991116	AU 1999-37484	19990415
EP 1073455	A1	20010207	EP 1999-919857	19990415
E: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002512377	T2	20020518	JP 2000-545557	19990415
PRIORITY APPL. INFO.:				
			US 1998-33472E	P 19980429
			WO 1999-US8303	W 19990415
REFERENCE COUNT:	5	THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE FE		

FORMAT

IT **Ribozymes**

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study);
 USES
 Uses.

compositions and methods for extending the action of clostridial
 neurotoxin

and modulating neurite outgrowth in damaged neural endplates)

IT 1:5544-55-2, Glycoprotein IGF-BP 4 (human clone HBP4-509 precursor
 protein.

moiety reduced) 136753-17-8, **Insulin-like
 growth factor-binding protein**

5 (human

RL: BAC (Biological activity or effector, except adverse); BPR

unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PRPC (Process); USES (Uses)
(amino acid sequence, compns. and methods for extending the action of clostridial neurotoxin and modulating neurite outgrowth in damaged neural endplates)

13 ANSWER 23 OF 42 USPATFULL

ACCESSION NUMBER: 1998:164109 USPATFULL

TITLE: TNF receptor death ligand proteins and inhibitors of ligand binding

INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schievella, Andrea R., Winchester, MA, United States
Graham, James, Somerville, MA, United States

PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5852173		19981222
APPLICATION INFO.:	US 1995-584901		19950916 (3)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now		

abandoned

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Walsh, Stephen

ASSISTANT EXAMINER: Kaufman, Claire M.

LEGAL REPRESENTATIVE: Sprunger, Suzanne A., Brown, Scott A., DesPosier, Thomas J.

NUMBER OF CLAIMS: 7

EXEMPLARY CLAIM: 7

NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 1355

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and a protein selected from the group consisting of **insulin-like growth**

factor binding protein-5 ("

IGFBP-5"), and fragments thereof having TNF-R1-DD

ligand protein activity. Such proteins may also be administered for inhibiting TNF-R death domain. . . .

DRWD FIG. 7 is an autoradiograph which demonstrates that an **antisense** oligonucleotide derived from the sequence of clone 3TW inhibits TNF-induced cPLA.sub.2 phosphorylation.

DETD The protein encoded by clone 20DD is identical to amino acids 87 to 272 of **insulin-like growth factor**

binding protein-5 ("IGFBP-

5"), a sequence for which was disclosed in J. Biol. Chem.

266:10646-10653 (1991) by Shimasaki et al., which is incorporated herein

by reference. The polynucleotide and amino acid sequences of

IGFBP-5 are set forth in SEQ ID NO:7 and SEQ ID NO:8.

respectively. Based upon the sequence identity between clone 20DD and

IGFBP-5, IGFBP 5 and certain

fragments thereof will exhibit TNF-R1 DD ligand binding activity (as defined herein).

DETD Due to the similarity of their sequences to the insulin growth factor binding protein ("**IGFBP-5**") and fragments thereof

which bind to the TNF-R death domain are proteins having TNF-R1-DD ligand protein activity as defined herein. . . .

DETD . . . homologues compared to Genbank and other databases.

Sequence of clone 3TW, which encodes "3TW" with identical sequence to

Shimasaki et al., J. Biol. Chem. 266:10646-10653 (1991)) were isolated. The clones "2DD," "3" and "20DD" were chosen for.

DETD TNF signaling can be established by lowering or eliminating the

expression of the ligands. These experiments can be performed using **antisense** expression or transgenic mice.

DETD An **antisense** oligonucleotide was derived from the sequence of clone 3TW. The **antisense** oligonucleotide was assayed to determine its ability to inhibit TNF-induced cPLA_{sub}2 phosphorylation.

FIG. 7 depicts the results of that experiment. . . . the antisense oligonucleotide (3TWAS) was compared with the full-length clone (3TWFL).

Flag-3TW full length (3TWFL:flag) and pED-flag vector (pEDflag). The **antisense** oligonucleotide inhibited phosphorylation.

LS ANSWER 24 OF 42 USPATFULL

ACCESSION NUMBER: 1998:157118 USPATFULL

TITLE: TNF receptor death domain ligand proteins and method to

identify inhibitors of ligand binding

INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States

Chen, Jennifer, Chestnut Hill, MA, United States

Schievella, Andrea R., Winchester, MA, United States

PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5849501		19981215
APPLICATION INFO.:	US 1995-494440		19950613 (8)
RELATED AFFLN. INFO.:	Continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Walsh, Stephen		
ASSISTANT EXAMINER:	Kaufman, Claire M.		
LEGAL REPRESENTATIVE:	Brown, Scott A., Sprunger, Suzanne A., DesRosier, Thomas J.		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 6 Drawing Page(s)		
LINE COUNT:	1687		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and a protein selected from the group consisting of **insulin-like growth**

factor binding protein-5 ("

IGFBP-5"), and fragments thereof having TNF-R1-DD

ligand protein activity. Such proteins may also be administered for inhibiting TNF-R death domain binding.

DETD The protein encoded by clone 20DD is identical to amino acids 87 to 272 of **insulin-like growth factor**

binding protein-5 ("IGFBP-

5", a sequence for which was disclosed in J. Biol. Chem.

266:10646-10653 (1991) by Shimasaki et al., which is incorporated herein

by reference. The polynucleotide and amino acid sequences of

IGFBP-5 are set forth in SEQ ID NO:7 and SEQ ID NO:8,

respectively. Based upon the sequence identity between clone 20DD and

IGFBP-5, **IGFBP-5** and certain

fragments thereof will exhibit TNF-R1-DD ligand binding activity (as defined herein).

DETD Due to the similarity of their sequences to the insulin growth factor

ligand protein activity as defined herein. . . .
 DETD homologies compared to Genbank and other databases.
 Additionally, four other clones ("20DD") with identical sequence to a
 portion of human **insulin-like growth**
factor binding protein-5 (Shunichi
 Shimasaki et al., J. Biol. Chem. 266:10646-10653 (1991)) were isolated.
 The clones "1DD," "3DD" and "20DD" were chosen for. . . .
 DETD TNF signaling can be established by lowering or eliminating
 the
 expression of the ligands. These experiments can be performed using
antisense expression or transgenic mice.

LS ANSWER 1 OF 41 USPTAFULL

ACCESSION NUMBER: 1999:194998 USPTAFULL
 TITLE: TNF receptor death domain ligand proteins
 INVENTOR S: Lin, Lin-Ling, Concord, MA, United States
 Chen, Jennifer, Chestnut Hill, MA, United States
 PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States
 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5947399		19991208
APPLICATION INFO.:	US 1996-649341		19960517 (2)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Walsh, Stephen		
ASSISTANT EXAMINER:	Kaufman, Claire M.		
LEGAL REPRESENTATIVE:	Brown, Scott A., DesRosier, Thomas J.		
NUMBER OF CLAIMS:	15		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)		
LINE COUNT:	1242		

CAS INDEXING IS AVAILAble FOR THIS PATENT.

SUMM therapeutically effective amount of a composition comprising a
 pharmaceutically acceptable carrier and a protein selected from the
 group consisting of **insulin-like growth**

factor binding protein-5 ("

IGFBP-5"), and fragments thereof having TNF-R1-DD

ligand protein activity. Such proteins may also be administered for
 inhibiting TNF-R death domain binding.

DETD The protein encoded by clone 20DD is identical to amino acids 97 to 272
 of **insulin-like growth factor**

binding protein-5 ("IGFBP-

5"), a sequence for which was disclosed in J. Biol. Chem.

266:10646-10653 (1991) by Shimasaki et al., which is incorporated
 herein

by reference. The polynucleotide and amino acid sequences of

IGFBP 5 are set forth in SEQ ID NO:7 and SEQ ID NO:8,

respectively. Based upon the sequence identity between clone 20DD and

IGFBP 5, **IGFBP 5** and certain

fragments thereof will exhibit TNF-R1-DD ligand binding activity as
 defined herein.

DETD Due to the similarity of their sequences to the insulin growth factor
 binding protein ("IGFBP 5") and fragments thereof

which bind to the TNF-R death domain are proteins having TNF-R1-DD
 ligand protein activity as defined herein. . . .

DETD homologies compared to Genbank and other databases.

Additionally, four other clones ("20DD") with identical sequence to a
 portion of human **insulin-like growth**

factor binding protein-5 (Shunichi

Shimasaki et al., J. Biol. Chem. 266:10646-10653 (1991)) were isolated.

expression of the ligands. These experiments can be performed using antisense expression of transgenic mice.

13 ANSWER 26 OF 42 USPATFULL

ACCESSION NUMBER: 1998:150692 USPATFULL

TITLE: TNF receptor death domain ligand proteins and inhibitors of ligand binding

INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schiavella, Andrea R., Winchester, MA, United States
Graham, James, Somerville, MA, United States

PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States
(U.S. Corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5843675		19981201
APPLICATION INFO.:	US 1994-001123		19960215 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-533901, filed on 26 Sep 1995 which is a continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Ulm, John		
LEGAL REPRESENTATIVE:	Sprunger, Suzanne A., Brown, Scott A.		
NUMBER OF CLAIMS:	16		
EXEMPLARY CLAIM:	6		
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)		
LINE COUNT:	2025		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and a protein selected from the group consisting of **insulin-like growth**

factor binding protein-5 ("

IGFBP-5"), and fragments thereof having TNF-R1-DD

ligand protein activity. Such proteins may also be administered for inhibiting TNF-R death domain binding.

DRWD FIG. 7 is an autoradiograph which demonstrates that an **antisense** oligonucleotide derived from the sequence of clone 3TW inhibits TNF-induced cPLA₂ subunit phosphorylation.

DETD The protein encoded by clone 20DD is identical to amino acids 97 to 272 of **insulin-like growth factor**

binding protein-5 ("IGFBP-

5"), a sequence for which was disclosed in J. Biol. Chem.

266:10646-10653 (1991) by Shimasaki et al., which is incorporated herein

by reference. The polynucleotide and amino acid sequences of

IGFBP 5 are set forth in SEQ ID NO:7 and SEQ ID NO:8,

respectively. Based upon the sequence identity between clone 20DD and

IGFBP 5, IGFBP-5 and certain

fragments thereof will exhibit TNF-R1-DD ligand binding activity (as defined herein).

DETD Due to the similarity of their sequences to the insulin growth factor binding protein ("IGFBP 5") and fragments thereof which bind to the TNF-R death domain are proteins having TNF-R1-DD ligand protein activity as defined herein. . . .

DETD . . . homologues compared to Genbank and other databases.

Additionally, four other clones ("20DD", with identical sequence to a portion of human **insulin-like growth**

factor binding protein-5 Shunichi

Shimasaki et al., J. Biol. Chem. 266:10646-10653 (1991)) were isolated. The clones "20DD", "11" and "12" were chosen for . . .

expression of the ligands. These experiments can be performed using **antisense** expression in transgenic mice.

DETAILED An **antisense** oligonucleotide was derived from the sequence of clone 3TW. The **antisense** oligonucleotide was assayed to determine its ability to inhibit TNF-induced cPLA₂ substrate phosphorylation.

FIG. 7 depicts the results of that experiment. . . . the antisense oligonucleotide (3TWAS) was compared with the full-length clone (3TWFL),

Flag-3TW full length (3TWFLflag) and pED-flag vector (pEDflag). The **antisense** oligonucleotide inhibited phosphorylation.

13 ANSWER 27 OF 42 USPATFULL

ACCESSION NUMBER: 1993:45043 USPATFULL

TITLE: Methods and reagents for the identification and regulation of senescence-related genes
INVENTOR(S): Linskens, Maarten H. H., Palo Alto, CA, United States
Hirsch, Kenneth S., Palo Alto, CA, United States
Villegant, Bryant, San Carlos, CA, United States
Feng, Junli, San Carlos, CA, United States
Pank, Walter, Union City, CA, United States
West, Michael David, Belmont, CA, United States
PATENT ASSIGNEE(S): Genin Corporation, Menlo Park, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE

PATENT INFORMATION:	US 5744300		19980423
APPLICATION INFO :	US 1994-235180		19941031 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-235180, filed on 19 Apr 1994, now patented, Pat. No. US 5580726 And Ser. No. US 1993-38766, filed on 24 Mar 1993, now patented, Pat. No. US 5489504		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Myers, Carla J.		
LEGAL REPRESENTATIVE:	Haster, Kevin Lyon & Lyon LLP		
NUMBER OF CLAIMS:	17		
EXEMPLARY CLAIM:	1		
LINE COUNT:	2409		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM no. 01M5:; MITHS (encodes mitochondrial RNA, band no. 02A2);
HUMTFPA (encodes human tissue factor, band no. 06E1); HUMIGFBP5
(encodes

human insulin-like growth factor

binding protein 5, band no. 07J1; band no.

11H1 corresponds to Genbank locus HUMIGFBP5X; HUMSGP3 (encodes human secretory granule core proteoglycan, also known. . . .

SUMM techniques of molecular biology, not only to express the mRNA or protein encoded by the gene but also to express **antisense** oligonucleotides or **ribozymes** that can be used to prevent deleterious expression of senescence-related genes. Those of skill in the art recognize that a. . . .

13 ANSWER 28 OF 42 USPATFULL

ACCESSION NUMBER: 1993:45042 USPATFULL

TITLE: MACH, a TNF receptor death domain ligand protein
INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schievella, Andrea K., Winchester, MA, United States
Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

PATENT INFORMATION: US 5712381 19980127
APPLICATION INFO.: US 6-698551 19961815 18
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-602228, filed
on 15 Feb 1996 which is a continuation-in-part of Ser.
No. US 1993-583901, filed on 28 Sep 1995 which is a
continuation-in-part of Ser. No. US 1995-494440, filed
on 10 Jun 1995 which is a continuation-in-part of Ser.
No. US 1994-327514, filed on 19 Oct 1994, now

abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Walsh, Stephen
ASSISTANT EXAMINER: Rajan, Mukil
LEGAL REPRESENTATIVE: Brown, Scott A., Sprunger, Suzanne A., DesRocher,
Thomas J.

NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1819

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . therapeutically effective amount of a composition comprising a
pharmaceutically acceptable carrier and a protein selected from the
group consisting of **insulin-like growth**

factor binding protein-5 ("

IGFBP-5"), and fragments thereof having TNF-R1-DD

ligand protein activity. Such proteins may also be administered for
inhibiting TNF-R death domain binding.

DRWD FIG. 7 is an autoradiograph which demonstrates that an **antisense**
oligonucleotide derived from the sequence of clone 3TW inhibits
TNF-induced cPLA.sub.2 phosphorylation.

DETD The protein encoded by clone 20DD is identical to amino acids 87 to 272
of **insulin-like growth factor**

binding protein-5 ("IGFBP-

5"), a sequence for which was disclosed in J. Biol. Chem.

266:10646-10653 (1991) by Shimasaki et al., which is incorporated

herein

by reference. The polynucleotide and amino acid sequences of

IGFBP-5 are set forth in SEQ ID NO:7 and SEQ ID NO:8,

respectively. Based upon the sequence identity between clone 20DD and

IGFBP-5, **IGFBP-5** and certain

fragments thereof will exhibit TNF-R1-DD ligand binding activity (as
defined herein).

DETD Due to the similarity of their sequences to the insulin growth factor
binding protein ("**IGFBP-5**") and fragments thereof
which bind to the TNF-R death domain are proteins having TNF-R1-DD
ligand protein activity as defined herein. . . .

DETD . . . homologies compared to Genbank and other databases.

Additionally, four other clones ("**20DD**") with identical sequence to a
portion of human **insulin-like growth**

factor binding protein-5 (Shimashi

Shimasaki et al., J. Biol. Chem. 266:10646-10653 (1991)) were isolated.

The clones "**2DD**," "**3DD**" and "**10DD**" were chosen for. . . .

DETD . . . TNF signaling can be established by lowering or eliminating
the

expression of the ligands. These experiments can be performed using

antisense expression or transgenic mice.

DETD An **antisense** oligonucleotide was derived from the sequence of
clone 3TW. The **antisense** oligonucleotide was assayed to
determine its ability to inhibit TNF-induced cPLA.sub.2
phosphorylation.

FIG. 7 depicts the results of that experiment. . . . the antisense
oligonucleotide (3TWAS) was compared with the full-length clone

3TWFL,

Flag-3TW full-length (3TWFLflag) and pFL flag vector (pFLflag). The

L# ANSWER 31 OF 42 MEDLINE
 ACCESSION NUMBER: 9727885 MEDLINE
 DOCUMENT NUMBER: 9727885 PubMed ID: 9133435
 TITLE: Insulin-like growth factor binding protein gene expression in the pregnant rat uterus and placenta.
 AUTHOR: Denro J A; Pintar J E
 CORPORATE SOURCE: Department of Anatomy and Cell Biology, Columbia University
 College of Physicians and Surgeons, New York, New York 10032, USA.
 CONTRAST NUMBER: NS21970 (NINDS)
 SOURCE: DEVELOPMENTAL BIOLOGY, (1997 Apr 15) 184 (2) 278-95.
 Journal code: E7T; 0372762. ISSN: 0012-1606.
 PUB. COUNTRY: United States
 Journal; Article: (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199706
 ENTRY DATE: Entered STN: 19970612
 Last Updated on STN: 19970612
 Entered Medline: 19970602

AB . . . example, IGFBP-1 is expressed in the inner circular layer shortly after implantation, and expression increases through late gestation. In contrast, **IGFBP-5** hybridization occurs over both myometrial layers before implantation, but decreases in intensity and spatial distribution as pregnancy proceeds. Finally, and. . .

CT . . .
 Hybridization
 Microscopy, Video
 Myometrium: ME, metabolism
 Nucleic Acid Hybridization
 Placenta: CY, cytology
 *Placenta: ME, metabolism
 Pregnancy
 Preimplantation Phase
 Protein Binding
RNA, Antisense: ME, metabolism
 RNA, Messenger: GE, genetics
 RNA, Messenger: ME, metabolism
 Rats
 Rats, Sprague-Dawley
 Receptors, Somatomedin: BI, biosynthesis
 *Receptors, . . .
 CN 0 (RNA, **Antisense**); 0 (RNA, Messenger); 0 (Receptors, Somatomedin)

L# ANSWER 32 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1997:972983 BIOSIS
 DOCUMENT NUMBER: EREV199799672186
 TITLE: In vitro and in vivo studies on the role of insulin-like growth factor binding protein-3, -4 and -5 on bone formation.
 AUTHOR(S): Kanzaki, S. (1); Mohan, S.; Ono, T. (1); Matsuoaka, Y. (1); Moriwake, T. (1); Tanaka, H. (1); Seino, Y. (1)
 CORPORATE SOURCE: (1) Dep. Pediatrics, Okayama Univ. Med. Sch., Okayama 7 Japan
 SOURCE: Hormone Research (Basel), (1997) Vol. 48, No. SUPPL. 2, pp. 16.
 Meeting Info.: 5th Joint Meeting of the European Society for Paediatric Endocrinology and the Lawson Wilkins Society
 for Pediatric Endocrinology, in Collaboration with the

for Pediatric Endocrinology and the Latin American Society
for Pediatric Endocrinology Stockholm, Sweden June 22-26,
1997

ISSN: 1301-0163.

DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English
IT . . .

SYSTEM: LYMPHATICS; BONE; BONE DISEASE; BONE MINERAL DENSITY; ENDOCRINE
FORMATION; INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3; INSULIN-LIKE
GROWTH FACTOR BINDING PROTEIN-3 **ANTISENSE** OLIGONUCLEOTIDE;
INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-4; INSULIN-LIKE GROWTH
FACTOR BINDING PROTEIN-4 **ANTISENSE** OLIGONUCLEOTIDE;
INSULIN-LIKE GROWTH FACTOR
BINDING PROTEIN-5; HYPOTENIA; SENSORY
SYSTEM; SKELETAL SYSTEM

LE ANSWER 33 OF 42 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:111-09 CAPLUS

DOCUMENT NUMBER: 124:270541

TITLE: Use of **antisense** nucleic acids/analog
inhibiting growth factor-mediated cell proliferation
for treatment of proliferative and/or inflammatory
skin disorders

INVENTOR(S): Werther, George Arthur; Wright, Christopher John
PATENT ASSIGNEE(S): Royal Children's Hospital Research Foundation,
Australia

SOURCE: ECT Int. Appl., 113 pp.
CODEN: PEXKDE

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2601636	A1	19960125	WO 1995-AU410	19950706
W:	AM, AT, AU, BE, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NI, NZ, PL, PT, PG, PU, SD, SE, SG, SI, SK, TJ, TM, TT			
FW:	KE, MW, SD, SE, US, AT, BE, CH, IE, DK, ES, FR, GB, GR, IE, IT, LJ, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2194366	AA	19960125	CA 1995-2194366	19950706
AU 9528753	A1	19960109	AU 1995-28753	19950706
AU 692274	B2	19930604		
EP 776210	A1	19970604	EP 1995-324110	19950706
F:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,			

SE

JP 11508296	T2	19980818	JP 1995-504013	19950706
US 5739041	A	19990727	US 1996-666392	19960820
US 6,4741	B1	20010004	US 1996-199996	19961125

PRIORITY APPLN. INFO.:

AT 1994-6723	A	19940706
WO 1995-AU410	W	19950706
US 1996-666392	A1	19960820

TI Use of **antisense** nucleic acids/analog inhibiting growth
factor-mediated cell proliferation for treatment of proliferative and/or
inflammatory skin disorders

AB The present invention relates generally to a method for the prophylaxis
and/or treatment of skin disorders, and in particular proliferative
and/or

inflammatory skin disorders, and to nucleic acids or nucleic acid analogs
useful for same. The present invention is particularly directed to mole.

stimulation of this layer of cells. The present invention contemplates, in a most preferred embodiment, a method for the prophylaxis and/or treatment of psoriasis. Phosphorothioate-linked oligonucleotide (18- and 24-mers) **antisense** to human insulin-like growth factor binding protein 3-encoding nucleic acid inhibited IGFBP-3 synthesis by HaCaT cells (human differentiated keratinocyte cell line).

ST skin disorder proliferative inflammatory treatment; **antisense** oligonucleotide inhibiting growth factor proliferation; insulin like growth factor **antisense** oligonucleotide; psoriasis treatment **antisense** oligonucleotide growth factor

IT Animal growth regulator receptors
 RL: MSC (Miscellaneous)
 (antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogues inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Skin, disease
 (proliferative or inflammatory; use of **antisense** nucleic acids/analogues inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Meloid
 Keratosis
 Psoriasis
 Seborrhea
 Skin, neoplasm
 Wart
 (use of **antisense** nucleic acids/analogues inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT **Ribozymes**
 RL: THU (Therapeutic use); BIDL (Biological study); USES (Uses)
 (use of **antisense** nucleic acids/analogues inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Proteins, specific or class
 RL: MSC (Miscellaneous)
 (IGF-BP-2 (insulin-like growth factor-binding protein 2), antagonism of cell proliferation related to; use of **antisense** nucleic acids/analogues inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Glycoproteins, specific or class
 RL: MSC (Miscellaneous)
 (IGF-BP-3 (insulin-like growth factor-binding protein 3), antagonism of cell proliferation related to; use of **antisense** nucleic acids/analogues inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Glycoproteins, specific or class
 RL: MSC (Miscellaneous)
 (IGF-BP-4 (insulin-like growth factor-binding protein 4), antagonism of cell proliferation related to; use of **antisense** nucleic acids/analogues inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Proteins, specific or class
 RL: MSC (Miscellaneous)
 (IGF-BP-5 (insulin-like growth factor binding protein 5 , antagonism of cell proliferation related to; use of **antisense** nucleic acids/analogues inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Glycoproteins, specific or class
 RL: MSC (Miscellaneous)
 (IGF-BP-6 (insulin-like growth factor-binding protein 6), antagonism of cell proliferation related to; use of **antisense** nucleic acids/analogues inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

treatment skin disorders)

IT Receptors
 RL: MSC (Miscellaneous)
 (animal growth regulator, antagonism of cell proliferation induced by;
 use of **antisense** nucleic acids/analogs inhibiting growth
 factor-mediated cell proliferation for treatment skin disorders)

IT Connective tissue
 (disease, scleroderma, use of **antisense** nucleic acids/analogs
 inhibiting growth factor-mediated cell proliferation for treatment
 skin disorders)

IT Skin, disease
 (actinoyosis, use of **antisense** nucleic acids/analogs
 inhibiting growth factor-mediated cell proliferation for treatment
 skin disorders)

IT Receptors
 RL: MSC (Miscellaneous)
 (insulin-like growth factor I, antagonism of cell proliferation
 induced by; use of **antisense** nucleic acids/analogs inhibiting growth
 factor-mediated cell proliferation for treatment skin disorders)

IT Proteins, specific tr class
 RL: MSC (Miscellaneous)
 (insulin-like growth factor-binding, antagonism of cell proliferation
 related to; use of **antisense** nucleic acids/analogs inhibiting
 growth factor-mediated cell proliferation for treatment skin
 disorders)

IT Lymphokines and Cytokines
 RL: MSC (Miscellaneous)
 (interleukin 1, antagonism of cell proliferation induced by; use of
antisense nucleic acids/analogs inhibiting growth
 factor-mediated cell proliferation for treatment skin disorders)

IT Lymphokines and Cytokines
 RL: MSC (Miscellaneous)
 (interleukin 4, antagonism of cell proliferation induced by; use of
antisense nucleic acids/analogs inhibiting growth
 factor-mediated cell proliferation for treatment skin disorders)

IT Lymphokines and Cytokines
 RL: MSC (Miscellaneous)
 (interleukin 6, antagonism of cell proliferation induced by; use of
antisense nucleic acids/analogs inhibiting growth
 factor-mediated cell proliferation for treatment skin disorders)

IT Lymphokines and Cytokines
 RL: MSC (Miscellaneous)
 (interleukin 3, antagonism of cell proliferation induced by; use of
antisense nucleic acids/analogs inhibiting growth
 factor-mediated cell proliferation for treatment skin disorders)

IT Nucleotides, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (oligo-, **antisense**; use of **antisense** nucleic
 acids/analogs inhibiting growth factor-mediated cell proliferation for
 treatment skin disorders)

IT Skin, disease
 (psoriasis, use of **antisense** nucleic acids/analogs
 inhibiting growth factor-mediated cell proliferation for treatment
 skin disorders)

IT Lymphokines and Cytokines
 RL: MSC (Miscellaneous)
 (tumor necrosis factor-.alpha., antagonism of cell proliferation
 induced by; use of **antisense** nucleic acids/analogs inhibiting
 growth factor mediated cell proliferation for treatment skin
 disorders)

(.alpha.-transforming growth factors, antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT 67763-96-6, Insulin-like growth factor I 106196-93-9, Basic fibroblast growth factor 148843-15-6, Fibroblast growth factor 7

RL: MSC (Miscellaneous)

(antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT 140029-74-9, GenBank M31159 140063-68-4, GenBank X04434 140079-08-9, GenBank X16302

RL: MSC (Miscellaneous)

(**antisense** oligonucleotides in relation to; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT 175333-53-6 175333-59-7 175338-60-0 175338-61-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)